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(71) Applicant (for all designated States except US): CORIXA
CORPORATION [US/US]; Suite 200, 1124 Columbia
Street, Seattle, WA 98104 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): XU, Jiangchun
[US/US]; 15805 SE 43rd Place, Bellevue, WA 98006

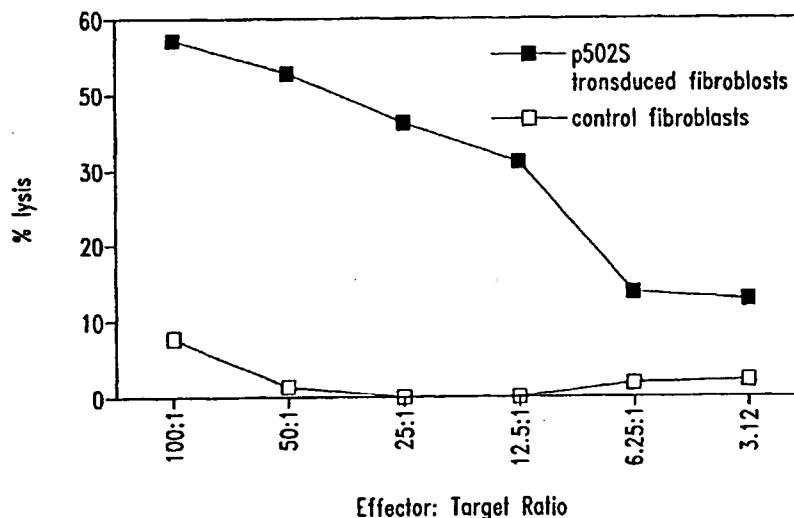
(US). DILLON, Davin, C. [US/US]; 18112 NW Mon-
treux Drive, Issaquah, WA 98027 (US). MITCHAM,
Jennifer, L. [US/US]; 16677 NE 88th Street, Redmond,
WA 98052 (US). HARLOCKER, Susan, L. [US/US];
7522 - 13th Avenue W., Seattle, WA 98117 (US). JIANG,
Yuqiu [CN/US]; 5001 South 232nd Street, Kent, WA
98032 (US). REED, Steven, G. [US/US]; 2843 - 122nd
Place NE, Bellevue, WA 98005 (US). KALOS, Michael,
D. [US/US]; 8116 Dayton Ave. N., Seattle, WA 98103
(US). RETTER, Marc, W. [US/US]; 33402 NE 43rd
Place, Carnation, WA 98014 (US). STOLK, John, A.
[US/US]; 7436 Northeast 144th Place, Bothell, WA 98011
(US). DAY, Craig, H. [US/US]; 11501 Stone Ave. N.,
C122, Seattle, WA 98133-8317 (US). SKEIKY, Yasir,
A.W. [CA/US]; 15106 SE 47th Place, Bellevue, WA 98006
(US). WANG, Aijun [CN/US]; 3106 213th Place. SE,
Issaquah, WA 98029 (US).

(74) Agents: POTTER, Jane, E., R.; Seed Intellectual Prop-
erty Law Group PLLC, Suite 6300, 701 Fifth Avenue, Seat-
tle, WA 98104-7092 et al. (US).

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[Continued on next page]

(54) Title: COMPOSITIONS AND METHODS FOR THE THERAPY AND DIAGNOSIS OF PROSTATE CANCER



(57) Abstract: Compositions and methods for the therapy and diagnosis of cancer, such as prostate cancer, are disclosed. Compositions may comprise one or more prostate-specific proteins, immunogenic portions thereof, or polynucleotides that encode such portions. Alternatively, a therapeutic composition may comprise an antigen presenting cell that expresses a prostate-specific protein, or a T cell that is specific for cells expressing such a protein. Such compositions may be used, for example, for the prevention and treatment of diseases such as prostate cancer. Diagnostic methods based on detecting a prostate-specific protein, or mRNA encoding such a protein, in a sample are also provided.

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COMPOSITIONS AND METHODS FOR THE THERAPY AND DIAGNOSIS OF PROSTATE CANCER

5 TECHNICAL FIELD

The present invention relates generally to therapy and diagnosis of cancer, such as prostate cancer. The invention is more specifically related to polypeptides comprising at least a portion of a prostate-specific protein, and to polynucleotides encoding such polypeptides. Such polypeptides and polynucleotides may be used in vaccines and pharmaceutical compositions for
10 prevention and treatment of prostate cancer, and for the diagnosis and monitoring of such cancers.

BACKGROUND OF THE INVENTION

Prostate cancer is the most common form of cancer among males, with an estimated incidence of 30% in men over the age of 50. Overwhelming clinical evidence shows that human prostate cancer has the propensity to metastasize to bone, and the disease appears to progress
15 inevitably from androgen dependent to androgen refractory status, leading to increased patient mortality. This prevalent disease is currently the second leading cause of cancer death among men in the U.S.

In spite of considerable research into therapies for the disease, prostate cancer remains difficult to treat. Commonly, treatment is based on surgery and/or radiation therapy, but
20 these methods are ineffective in a significant percentage of cases. Two previously identified prostate specific proteins - prostate specific antigen (PSA) and prostatic acid phosphatase (PAP) - have limited therapeutic and diagnostic potential. For example, PSA levels do not always correlate well with the presence of prostate cancer, being positive in a percentage of non-prostate cancer cases, including benign prostatic hyperplasia (BPH). Furthermore, PSA measurements correlate
25 with prostate volume, and do not indicate the level of metastasis.

In spite of considerable research into therapies for these and other cancers, prostate cancer remains difficult to diagnose and treat effectively. Accordingly, there is a need in the art for improved methods for detecting and treating such cancers. The present invention fulfills these needs and further provides other related advantages.

30 SUMMARY OF THE INVENTION

Briefly stated, the present invention provides compositions and methods for the

diagnosis and therapy of cancer, such as prostate cancer. In one aspect, the present invention provides polypeptides comprising at least a portion of a prostate-specific protein, or a variant thereof. Certain portions and other variants are immunogenic, such that the ability of the variant to react with antigen-specific antisera is not substantially diminished. Within certain embodiments, the polypeptide comprises at least an immunogenic portion of a prostate-specific protein, or a variant thereof, wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of: (a) sequences recited in any one of SEQ ID NOs: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382, 384-476, 524, 526, 530, 531, 533, 535 and 536; (b) sequences that hybridize to any of the foregoing sequences under moderately stringent conditions; and (c) complements of any of the sequence of (a) or (b). In certain specific embodiments, such a polypeptide comprises at least a portion, or variant thereof, of a protein that includes an amino acid sequence selected from the group consisting of sequences recited in any one of SEQ ID NO: 112-114, 172, 176, 178, 327, 329, 331, 336, 339, 376-380, 383, 477-483, 496, 504, 505, 519, 520, 522, 525, 527, 532, 534, 537-550.

The present invention further provides polynucleotides that encode a polypeptide as described above, or a portion thereof (such as a portion encoding at least 15 amino acid residues of a prostate-specific protein), expression vectors comprising such polynucleotides and host cells transformed or transfected with such expression vectors.

Within other aspects, the present invention provides pharmaceutical compositions comprising a polypeptide or polynucleotide as described above and a physiologically acceptable carrier.

Within a related aspect of the present invention, vaccines for prophylactic or therapeutic use are provided. Such vaccines comprise a polypeptide or polynucleotide as described above and an immunostimulant.

The present invention further provides pharmaceutical compositions that comprise: (a) an antibody or antigen-binding fragment thereof that specifically binds to a prostate-specific protein; and (b) a physiologically acceptable carrier. In certain embodiments, the present invention provides monoclonal antibodies that specifically bind to an amino acid sequence selected from the group consisting of SEQ ID NO: 496, 504, 505, 509-517, 522 and 541-550, together with monoclonal antibodies comprising a complementarity determining region selected from the group consisting of SEQ ID NO: 502, 503 and 506-508.

Within further aspects, the present invention provides pharmaceutical compositions comprising: (a) an antigen presenting cell that expresses a polypeptide as described above and (b) a pharmaceutically acceptable carrier or excipient. Antigen presenting cells include dendritic cells, macrophages, monocytes, fibroblasts and B cells.

5 Within related aspects, vaccines are provided that comprise: (a) an antigen presenting cell that expresses a polypeptide as described above and (b) an immunostimulant.

The present invention further provides, in other aspects, fusion proteins that comprise at least one polypeptide as described above, as well as polynucleotides encoding such fusion proteins.

10 Within related aspects, pharmaceutical compositions comprising a fusion protein, or a polynucleotide encoding a fusion protein, in combination with a physiologically acceptable carrier are provided.

Vaccines are further provided, within other aspects, that comprise a fusion protein, or a polynucleotide encoding a fusion protein, in combination with an immunostimulant.

15 Within further aspects, the present invention provides methods for inhibiting the development of a cancer in a patient, comprising administering to a patient a pharmaceutical composition or vaccine as recited above.

The present invention further provides, within other aspects, methods for removing tumor cells from a biological sample, comprising contacting a biological sample with T cells that specifically react with a prostate-specific protein, wherein the step of contacting is performed under conditions and for a time sufficient to permit the removal of cells expressing the protein from the sample.

20 Within related aspects, methods are provided for inhibiting the development of a cancer in a patient, comprising administering to a patient a biological sample treated as described above.

25 Methods are further provided, within other aspects, for stimulating and/or expanding T cells specific for a prostate-specific protein, comprising contacting T cells with one or more of: (i) a polypeptide as described above; (ii) a polynucleotide encoding such a polypeptide; and/or (iii) an antigen presenting cell that expresses such a polypeptide; under conditions and for a time sufficient to permit the stimulation and/or expansion of T cells. Isolated T cell populations comprising T cells prepared as described above are also provided.

Within further aspects, the present invention provides methods for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a T cell population as described above.

The present invention further provides methods for inhibiting the development of a cancer in a patient, comprising the steps of: (a) incubating CD4⁺ and/or CD8⁺ T cells isolated from a patient with one or more of: (i) a polypeptide comprising at least an immunogenic portion of a prostate-specific protein; (ii) a polynucleotide encoding such a polypeptide; and (iii) an antigen-presenting cell that expressed such a polypeptide; and (b) administering to the patient an effective amount of the proliferated T cells, and thereby inhibiting the development of a cancer in the patient.

10 Proliferated cells may, but need not, be cloned prior to administration to the patient.

Within further aspects, the present invention provides methods for determining the presence or absence of a cancer in a patient, comprising: (a) contacting a biological sample obtained from a patient with a binding agent that binds to a polypeptide as recited above; (b) detecting in the sample an amount of polypeptide that binds to the binding agent; and (c) comparing the amount of polypeptide with a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient. Within preferred embodiments, the binding agent is an antibody, more preferably a monoclonal antibody. The cancer may be prostate cancer.

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The present invention also provides, within other aspects, methods for monitoring the progression of a cancer in a patient. Such methods comprise the steps of: (a) contacting a biological sample obtained from a patient at a first point in time with a binding agent that binds to a polypeptide as recited above; (b) detecting in the sample an amount of polypeptide that binds to the binding agent; (c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and (d) comparing the amount of polypeptide detected in step (c) with the amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.

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The present invention further provides, within other aspects, methods for determining the presence or absence of a cancer in a patient, comprising the steps of: (a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes a prostate-specific protein; (b) detecting in the sample a level of a polynucleotide, preferably mRNA, that hybridizes to the oligonucleotide; and (c) comparing the level of polynucleotide that hybridizes to the oligonucleotide with a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient. Within certain

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embodiments, the amount of mRNA is detected via polymerase chain reaction using, for example, at least one oligonucleotide primer that hybridizes to a polynucleotide encoding a polypeptide as recited above, or a complement of such a polynucleotide. Within other embodiments, the amount of mRNA is detected using a hybridization technique, employing an oligonucleotide probe that
5 hybridizes to a polynucleotide that encodes a polypeptide as recited above, or a complement of such a polynucleotide.

In related aspects, methods are provided for monitoring the progression of a cancer in a patient, comprising the steps of: (a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes a prostate-specific protein; (b)
10 detecting in the sample an amount of a polynucleotide that hybridizes to the oligonucleotide; (c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and (d) comparing the amount of polynucleotide detected in step (c) with the amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.

Within further aspects, the present invention provides antibodies, such as
15 monoclonal antibodies, that bind to a polypeptide as described above, as well as diagnostic kits comprising such antibodies. Diagnostic kits comprising one or more oligonucleotide probes or primers as described above are also provided.

These and other aspects of the present invention will become apparent upon reference to the following detailed description and attached drawings. All references disclosed
20 herein are hereby incorporated by reference in their entirety as if each was incorporated individually.

BRIEF DESCRIPTION OF THE DRAWINGS AND SEQUENCE IDENTIFIERS

Figure 1 illustrates the ability of T cells to kill fibroblasts expressing the representative prostate-specific polypeptide P502S, as compared to control fibroblasts. The
25 percentage lysis is shown as a series of effector:target ratios, as indicated.

Figures 2A and 2B illustrate the ability of T cells to recognize cells expressing the representative prostate-specific polypeptide P502S. In each case, the number of γ -interferon spots is shown for different numbers of responders. In Figure 2A, data is presented for fibroblasts pulsed with the P2S-12 peptide, as compared to fibroblasts pulsed with a control E75 peptide. In Figure
30 2B, data is presented for fibroblasts expressing P502S, as compared to fibroblasts expressing HER-2/neu.

Figure 3 represents a peptide competition binding assay showing that the P1S#10 peptide, derived from P501S, binds HLA-A2. Peptide P1S#10 inhibits HLA-A2 restricted presentation of fluM58 peptide to CTL clone D150M58 in TNF release bioassay. D150M58 CTL is specific for the HLA-A2 binding influenza matrix peptide fluM58.

5 Figure 4 illustrates the ability of T cell lines generated from P1S#10 immunized mice to specifically lyse P1S#10-pulsed Jurkat A2Kb targets and P501S-transduced Jurkat A2Kb targets, as compared to EGFP-transduced Jurkat A2Kb. The percent lysis is shown as a series of effector to target ratios, as indicated.

10 Figure 5 illustrates the ability of a T cell clone to recognize and specifically lyse Jurkat A2Kb cells expressing the representative prostate-specific polypeptide P501S, thereby demonstrating that the P1S#10 peptide may be a naturally processed epitope of the P501S polypeptide.

Figures 6A and 6B are graphs illustrating the specificity of a CD8⁺ cell line (3A-1) for a representative prostate-specific antigen (P501S). Figure 6A shows the results of a ⁵¹Cr release assay. The percent specific lysis is shown as a series of effector:target ratios, as indicated. Figure 6B shows the production of interferon-gamma by 3A-1 cells stimulated with autologous B-LCL transduced with P501S, at varying effector:target ratios as indicated.

Figure 7 is a Western blot showing the expression of P501S in baculovirus.

Figure 8 illustrates the results of epitope mapping studies on P501S.

20 Figure 9 is a schematic representation of the P501S protein showing the location of transmembrane domains and predicted intracellular and extracellular domains.

Figure 10 is a genomic map showing the location of the prostate genes P775P, P704P, B305D, P712P and P774P within the Cat Eye Syndrome region of chromosome 22q11.2

25 Figure 11 shows the results of an ELISA assay of antibody specificity to P501S peptides.

SEQ ID NO: 1 is the determined cDNA sequence for F1-13

SEQ ID NO: 2 is the determined 3' cDNA sequence for F1-12

SEQ ID NO: 3 is the determined 5' cDNA sequence for F1-12

SEQ ID NO: 4 is the determined 3' cDNA sequence for F1-16

30 SEQ ID NO: 5 is the determined 3' cDNA sequence for H1-1

SEQ ID NO: 6 is the determined 3' cDNA sequence for H1-9

SEQ ID NO: 7 is the determined 3' cDNA sequence for H1-4

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SEQ ID NO: 10 is the determined 3' cDNA sequence for L1-12
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SEQ ID NO: 30 is the determined 3' cDNA sequence for J1-12
SEQ ID NO: 31 is the determined 3' cDNA sequence for J1-16
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SEQ ID NO: 33 is the determined 3' cDNA sequence for K1-48
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SEQ ID NO: 35 is the determined 3' cDNA sequence for L1-2
SEQ ID NO: 36 is the determined 3' cDNA sequence for L1-6
30 SEQ ID NO: 37 is the determined 3' cDNA sequence for N1-1858
SEQ ID NO: 38 is the determined 3' cDNA sequence for N1-1860
SEQ ID NO: 39 is the determined 3' cDNA sequence for N1-1861

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SEQ ID NO: 104 is the determined cDNA sequence for 1D-4304

SEQ ID NO: 105 is the determined cDNA sequence for 1D-4296

SEQ ID NO: 106 is the determined cDNA sequence for 1D-4280

SEQ ID NO: 107 is the determined full length cDNA sequence for F1-12 (also referred to as P504S)

5

SEQ ID NO: 108 is the predicted amino acid sequence for F1-12

SEQ ID NO: 109 is the determined full length cDNA sequence for J1-17

SEQ ID NO: 110 is the determined full length cDNA sequence for L1-12 (also referred to as P501S)

SEQ ID NO: 111 is the determined full length cDNA sequence for N1-1862 (also referred to as

10 P503S)

SEQ ID NO: 112 is the predicted amino acid sequence for J1-17

SEQ ID NO: 113 is the predicted amino acid sequence for L1-12 (also referred to as P501S)

SEQ ID NO: 114 is the predicted amino acid sequence for N1-1862 (also referred to as P503S)

SEQ ID NO: 115 is the determined cDNA sequence for P89

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- SEQ ID NO: 171 is the determined cDNA sequence for P703P-DE1
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- SEQ ID NO: 194 is the determined extended cDNA sequence for 1G-4761
- 30 SEQ ID NO: 195 is the determined extended cDNA sequence for 1G-4762
- SEQ ID NO: 196 is the determined extended cDNA sequence for 1H-4766
- SEQ ID NO: 197 is the determined 3' cDNA sequence for 1H-4770

- SEQ ID NO: 198 is the determined 3' cDNA sequence for 1H-4771
SEQ ID NO: 199 is the determined extended cDNA sequence for 1H-4772
SEQ ID NO: 200 is the determined extended cDNA sequence for 1D-4309
SEQ ID NO: 201 is the determined extended cDNA sequence for 1D.1-4278
5 SEQ ID NO: 202 is the determined extended cDNA sequence for 1D-4288
SEQ ID NO: 203 is the determined extended cDNA sequence for 1D-4283
SEQ ID NO: 204 is the determined extended cDNA sequence for 1D-4304
SEQ ID NO: 205 is the determined extended cDNA sequence for 1D-4296
SEQ ID NO: 206 is the determined extended cDNA sequence for 1D-4280
10 SEQ ID NO: 207 is the determined cDNA sequence for 10-d8fwd
SEQ ID NO: 208 is the determined cDNA sequence for 10-H10con
SEQ ID NO: 209 is the determined cDNA sequence for 11-C8rev
SEQ ID NO: 210 is the determined cDNA sequence for 7.g6fwd
SEQ ID NO: 211 is the determined cDNA sequence for 7.g6rev
15 SEQ ID NO: 212 is the determined cDNA sequence for 8-b5fwd
SEQ ID NO: 213 is the determined cDNA sequence for 8-b5rev
SEQ ID NO: 214 is the determined cDNA sequence for 8-b6fwd
SEQ ID NO: 215 is the determined cDNA sequence for 8-b6 rev
SEQ ID NO: 216 is the determined cDNA sequence for 8-d4fwd
20 SEQ ID NO: 217 is the determined cDNA sequence for 8-d9rev
SEQ ID NO: 218 is the determined cDNA sequence for 8-g3fwd
SEQ ID NO: 219 is the determined cDNA sequence for 8-g3rev
SEQ ID NO: 220 is the determined cDNA sequence for 8-h11rev
SEQ ID NO: 221 is the determined cDNA sequence for g-f12fwd
25 SEQ ID NO: 222 is the determined cDNA sequence for g-f3rev
SEQ ID NO: 223 is the determined cDNA sequence for P509S
SEQ ID NO: 224 is the determined cDNA sequence for P510S
SEQ ID NO: 225 is the determined cDNA sequence for P703DE5
SEQ ID NO: 226 is the determined cDNA sequence for 9-A11
30 SEQ ID NO: 227 is the determined cDNA sequence for 8-C6
SEQ ID NO: 228 is the determined cDNA sequence for 8-H7
SEQ ID NO: 229 is the determined cDNA sequence for JPTPN13

- SEQ ID NO: 230 is the determined cDNA sequence for JPTPN14
SEQ ID NO: 231 is the determined cDNA sequence for JPTPN23
SEQ ID NO: 232 is the determined cDNA sequence for JPTPN24
SEQ ID NO: 233 is the determined cDNA sequence for JPTPN25
5 SEQ ID NO: 234 is the determined cDNA sequence for JPTPN30
SEQ ID NO: 235 is the determined cDNA sequence for JPTPN34
SEQ ID NO: 236 is the determined cDNA sequence for PTPN35
SEQ ID NO: 237 is the determined cDNA sequence for JPTPN36
SEQ ID NO: 238 is the determined cDNA sequence for JPTPN38
10 SEQ ID NO: 239 is the determined cDNA sequence for JPTPN39
SEQ ID NO: 240 is the determined cDNA sequence for JPTPN40
SEQ ID NO: 241 is the determined cDNA sequence for JPTPN41
SEQ ID NO: 242 is the determined cDNA sequence for JPTPN42
SEQ ID NO: 243 is the determined cDNA sequence for JPTPN45
15 SEQ ID NO: 244 is the determined cDNA sequence for JPTPN46
SEQ ID NO: 245 is the determined cDNA sequence for JPTPN51
SEQ ID NO: 246 is the determined cDNA sequence for JPTPN56
SEQ ID NO: 247 is the determined cDNA sequence for PTPN64
SEQ ID NO: 248 is the determined cDNA sequence for JPTPN65
20 SEQ ID NO: 249 is the determined cDNA sequence for JPTPN67
SEQ ID NO: 250 is the determined cDNA sequence for JPTPN76
SEQ ID NO: 251 is the determined cDNA sequence for JPTPN84
SEQ ID NO: 252 is the determined cDNA sequence for JPTPN85
SEQ ID NO: 253 is the determined cDNA sequence for JPTPN86
25 SEQ ID NO: 254 is the determined cDNA sequence for JPTPN87
SEQ ID NO: 255 is the determined cDNA sequence for JPTPN88
SEQ ID NO: 256 is the determined cDNA sequence for JP1F1
SEQ ID NO: 257 is the determined cDNA sequence for JP1F2
SEQ ID NO: 258 is the determined cDNA sequence for JP1C2
30 SEQ ID NO: 259 is the determined cDNA sequence for JP1B1
SEQ ID NO: 260 is the determined cDNA sequence for JP1B2
SEQ ID NO: 261 is the determined cDNA sequence for JP1D3

- SEQ ID NO: 262 is the determined cDNA sequence for JP1A4
SEQ ID NO: 263 is the determined cDNA sequence for JP1F5
SEQ ID NO: 264 is the determined cDNA sequence for JP1E6
SEQ ID NO: 265 is the determined cDNA sequence for JP1D6
5 SEQ ID NO: 266 is the determined cDNA sequence for JP1B5
SEQ ID NO: 267 is the determined cDNA sequence for JP1A6
SEQ ID NO: 268 is the determined cDNA sequence for JP1E8
SEQ ID NO: 269 is the determined cDNA sequence for JP1D7
SEQ ID NO: 270 is the determined cDNA sequence for JP1D9
10 SEQ ID NO: 271 is the determined cDNA sequence for JP1C10
SEQ ID NO: 272 is the determined cDNA sequence for JP1A9
SEQ ID NO: 273 is the determined cDNA sequence for JP1F12
SEQ ID NO: 274 is the determined cDNA sequence for JP1E12
SEQ ID NO: 275 is the determined cDNA sequence for JP1D11
15 SEQ ID NO: 276 is the determined cDNA sequence for JP1C11
SEQ ID NO: 277 is the determined cDNA sequence for JP1C12
SEQ ID NO: 278 is the determined cDNA sequence for JP1B12
SEQ ID NO: 279 is the determined cDNA sequence for JP1A12
SEQ ID NO: 280 is the determined cDNA sequence for JP8G2
20 SEQ ID NO: 281 is the determined cDNA sequence for JP8H1
SEQ ID NO: 282 is the determined cDNA sequence for JP8H2
SEQ ID NO: 283 is the determined cDNA sequence for JP8A3
SEQ ID NO: 284 is the determined cDNA sequence for JP8A4
SEQ ID NO: 285 is the determined cDNA sequence for JP8C3
25 SEQ ID NO: 286 is the determined cDNA sequence for JP8G4
SEQ ID NO: 287 is the determined cDNA sequence for JP8B6
SEQ ID NO: 288 is the determined cDNA sequence for JP8D6
SEQ ID NO: 289 is the determined cDNA sequence for JP8F5
SEQ ID NO: 290 is the determined cDNA sequence for JP8A8
30 SEQ ID NO: 291 is the determined cDNA sequence for JP8C7
SEQ ID NO: 292 is the determined cDNA sequence for JP8D7
SEQ ID NO: 293 is the determined cDNA sequence for P8D8

- SEQ ID NO: 294 is the determined cDNA sequence for JP8E7
SEQ ID NO: 295 is the determined cDNA sequence for JP8F8
SEQ ID NO: 296 is the determined cDNA sequence for JP8G8
SEQ ID NO: 297 is the determined cDNA sequence for JP8B10
5 SEQ ID NO: 298 is the determined cDNA sequence for JP8C10
SEQ ID NO: 299 is the determined cDNA sequence for JP8E9
SEQ ID NO: 300 is the determined cDNA sequence for JP8E10
SEQ ID NO: 301 is the determined cDNA sequence for JP8F9
SEQ ID NO: 302 is the determined cDNA sequence for JP8H9
10 SEQ ID NO: 303 is the determined cDNA sequence for JP8C12
SEQ ID NO: 304 is the determined cDNA sequence for JP8E11
SEQ ID NO: 305 is the determined cDNA sequence for JP8E12
SEQ ID NO: 306 is the amino acid sequence for the peptide PS2#12
SEQ ID NO: 307 is the determined cDNA sequence for P711P
15 SEQ ID NO: 308 is the determined cDNA sequence for P712P
SEQ ID NO: 309 is the determined cDNA sequence for CLONE23
SEQ ID NO: 310 is the determined cDNA sequence for P774P
SEQ ID NO: 311 is the determined cDNA sequence for P775P
SEQ ID NO: 312 is the determined cDNA sequence for P715P
20 SEQ ID NO: 313 is the determined cDNA sequence for P710P
SEQ ID NO: 314 is the determined cDNA sequence for P767P
SEQ ID NO: 315 is the determined cDNA sequence for P768P
SEQ ID NO: 316-325 are the determined cDNA sequences of previously isolated genes
SEQ ID NO: 326 is the determined cDNA sequence for P703PDE5
25 SEQ ID NO: 327 is the predicted amino acid sequence for P703PDE5
SEQ ID NO: 328 is the determined cDNA sequence for P703P6.26
SEQ ID NO: 329 is the predicted amino acid sequence for P703P6.26
SEQ ID NO: 330 is the determined cDNA sequence for P703PX-23
SEQ ID NO: 331 is the predicted amino acid sequence for P703PX-23
30 SEQ ID NO: 332 is the determined full length cDNA sequence for P509S
SEQ ID NO: 333 is the determined extended cDNA sequence for P707P (also referred to as 11-C9)
SEQ ID NO: 334 is the determined cDNA sequence for P714P

- SEQ ID NO: 335 is the determined cDNA sequence for P705P (also referred to as 9-F3)
- SEQ ID NO: 336 is the predicted amino acid sequence for P705P
- SEQ ID NO: 337 is the amino acid sequence of the peptide P1S#10
- SEQ ID NO: 338 is the amino acid sequence of the peptide p5
- 5 SEQ ID NO: 339 is the predicted amino acid sequence of P509S
- SEQ ID NO: 340 is the determined cDNA sequence for P778P
- SEQ ID NO: 341 is the determined cDNA sequence for P786P
- SEQ ID NO: 342 is the determined cDNA sequence for P789P
- SEQ ID NO: 343 is the determined cDNA sequence for a clone showing homology to Homo
- 10 sapiens MM46 mRNA
- SEQ ID NO: 344 is the determined cDNA sequence for a clone showing homology to Homo sapiens TNF-alpha stimulated ABC protein (ABC50) mRNA
- SEQ ID NO: 345 is the determined cDNA sequence for a clone showing homology to Homo sapiens mRNA for E-cadherin
- 15 SEQ ID NO: 346 is the determined cDNA sequence for a clone showing homology to Human nuclear-encoded mitochondrial serine hydroxymethyltransferase (SHMT)
- SEQ ID NO: 347 is the determined cDNA sequence for a clone showing homology to Homo sapiens natural resistance-associated macrophage protein2 (NRAMP2)
- SEQ ID NO: 348 is the determined cDNA sequence for a clone showing homology to Homo
- 20 sapiens phosphoglucomutase-related protein (PGMRP)
- SEQ ID NO: 349 is the determined cDNA sequence for a clone showing homology to Human mRNA for proteosome subunit p40
- SEQ ID NO: 350 is the determined cDNA sequence for P777P
- SEQ ID NO: 351 is the determined cDNA sequence for P779P
- 25 SEQ ID NO: 352 is the determined cDNA sequence for P790P
- SEQ ID NO: 353 is the determined cDNA sequence for P784P
- SEQ ID NO: 354 is the determined cDNA sequence for P776P
- SEQ ID NO: 355 is the determined cDNA sequence for P780P
- SEQ ID NO: 356 is the determined cDNA sequence for P544S
- 30 SEQ ID NO: 357 is the determined cDNA sequence for P745S
- SEQ ID NO: 358 is the determined cDNA sequence for P782P
- SEQ ID NO: 359 is the determined cDNA sequence for P783P

- SEQ ID NO: 360 is the determined cDNA sequence for unknown 17984
- SEQ ID NO: 361 is the determined cDNA sequence for P787P
- SEQ ID NO: 362 is the determined cDNA sequence for P788P
- SEQ ID NO: 363 is the determined cDNA sequence for unknown 17994
- 5 SEQ ID NO: 364 is the determined cDNA sequence for P781P
- SEQ ID NO: 365 is the determined cDNA sequence for P785P
- SEQ ID NO: 366-375 are the determined cDNA sequences for splice variants of B305D.
- SEQ ID NO: 376 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: 366.
- 10 SEQ ID NO: 377 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: 372.
- SEQ ID NO: 378 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: 373.
- SEQ ID NO: 379 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: 374.
- 15 SEQ ID NO: 380 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: 375.
- SEQ ID NO: 381 is the determined cDNA sequence for B716P.
- SEQ ID NO: 382 is the determined full-length cDNA sequence for P711P.
- 20 SEQ ID NO: 383 is the predicted amino acid sequence for P711P.
- SEQ ID NO: 384 is the cDNA sequence for P1000C.
- SEQ ID NO: 385 is the cDNA sequence for CGI-82.
- SEQ ID NO: 386 is the cDNA sequence for 23320.
- SEQ ID NO: 387 is the cDNA sequence for CGI-69.
- 25 SEQ ID NO: 388 is the cDNA sequence for L-iditol-2-dehydrogenase.
- SEQ ID NO: 389 is the cDNA sequence for 23379.
- SEQ ID NO: 390 is the cDNA sequence for 23381.
- SEQ ID NO: 391 is the cDNA sequence for KIAA0122.
- SEQ ID NO: 392 is the cDNA sequence for 23399.
- 30 SEQ ID NO: 393 is the cDNA sequence for a previously identified gene.
- SEQ ID NO: 394 is the cDNA sequence for HCLBP.
- SEQ ID NO: 395 is the cDNA sequence for transglutaminase.

SEQ ID NO:396 is the cDNA sequence for a previously identified gene.

SEQ ID NO:397 is the cDNA sequence for PAP.

SEQ ID NO:398 is the cDNA sequence for Ets transcription factor PDEF.

SEQ ID NO:399 is the cDNA sequence for hTGR.

5 SEQ ID NO:400 is the cDNA sequence for KIAA0295.

SEQ ID NO:401 is the cDNA sequence for 22545.

SEQ ID NO:402 is the cDNA sequence for 22547.

SEQ ID NO:403 is the cDNA sequence for 22548.

SEQ ID NO:404 is the cDNA sequence for 22550.

10 SEQ ID NO:405 is the cDNA sequence for 22551.

SEQ ID NO:406 is the cDNA sequence for 22552.

SEQ ID NO:407 is the cDNA sequence for 22553.

SEQ ID NO:408 is the cDNA sequence for 22558.

SEQ ID NO:409 is the cDNA sequence for 22562.

15 SEQ ID NO:410 is the cDNA sequence for 22565.

SEQ ID NO:411 is the cDNA sequence for 22567.

SEQ ID NO:412 is the cDNA sequence for 22568.

SEQ ID NO:413 is the cDNA sequence for 22570.

SEQ ID NO:414 is the cDNA sequence for 22571.

20 SEQ ID NO:415 is the cDNA sequence for 22572.

SEQ ID NO:416 is the cDNA sequence for 22573.

SEQ ID NO:417 is the cDNA sequence for 22573.

SEQ ID NO:418 is the cDNA sequence for 22575.

SEQ ID NO:419 is the cDNA sequence for 22580.

25 SEQ ID NO:420 is the cDNA sequence for 22581.

SEQ ID NO:421 is the cDNA sequence for 22582.

SEQ ID NO:422 is the cDNA sequence for 22583.

SEQ ID NO:423 is the cDNA sequence for 22584.

SEQ ID NO:424 is the cDNA sequence for 22585.

30 SEQ ID NO:425 is the cDNA sequence for 22586.

SEQ ID NO:426 is the cDNA sequence for 22587.

SEQ ID NO:427 is the cDNA sequence for 22588.

- SEQ ID NO:428 is the cDNA sequence for 22589.
SEQ ID NO:429 is the cDNA sequence for 22590.
SEQ ID NO:430 is the cDNA sequence for 22591.
SEQ ID NO:431 is the cDNA sequence for 22592.
5 SEQ ID NO:432 is the cDNA sequence for 22593.
SEQ ID NO:433 is the cDNA sequence for 22594.
SEQ ID NO:434 is the cDNA sequence for 22595.
SEQ ID NO:435 is the cDNA sequence for 22596.
SEQ ID NO:436 is the cDNA sequence for 22847.
10 SEQ ID NO:437 is the cDNA sequence for 22848.
SEQ ID NO:438 is the cDNA sequence for 22849.
SEQ ID NO:439 is the cDNA sequence for 22851.
SEQ ID NO:440 is the cDNA sequence for 22852.
SEQ ID NO:441 is the cDNA sequence for 22853.
15 SEQ ID NO:442 is the cDNA sequence for 22854.
SEQ ID NO:443 is the cDNA sequence for 22855.
SEQ ID NO:444 is the cDNA sequence for 22856.
SEQ ID NO:445 is the cDNA sequence for 22857.
SEQ ID NO:446 is the cDNA sequence for 23601.
20 SEQ ID NO:447 is the cDNA sequence for 23602.
SEQ ID NO:448 is the cDNA sequence for 23605.
SEQ ID NO:449 is the cDNA sequence for 23606.
SEQ ID NO:450 is the cDNA sequence for 23612.
SEQ ID NO:451 is the cDNA sequence for 23614.
25 SEQ ID NO:452 is the cDNA sequence for 23618.
SEQ ID NO:453 is the cDNA sequence for 23622.
SEQ ID NO:454 is the cDNA sequence for folate hydrolase.
SEQ ID NO:455 is the cDNA sequence for LIM protein.
SEQ ID NO:456 is the cDNA sequence for a known gene.
30 SEQ ID NO:457 is the cDNA sequence for a known gene.
SEQ ID NO:458 is the cDNA sequence for a previously identified gene.
SEQ ID NO:459 is the cDNA sequence for 23045.

- SEQ ID NO:460 is the cDNA sequence for 23032.
- SEQ ID NO:461 is the cDNA sequence for 23054.
- SEQ ID NO:462-467 are cDNA sequences for known genes.
- SEQ ID NO:468-471 are cDNA sequences for P710P.
- 5 SEQ ID NO:472 is a cDNA sequence for P1001C.
- SEQ ID NO: 473 is the determined cDNA sequence for a first splice variant of P775P (referred to as 27505).
- SEQ ID NO: 474 is the determined cDNA sequence for a second splice variant of P775P (referred to as 19947).
- 10 SEQ ID NO: 475 is the determined cDNA sequence for a third splice variant of P775P (referred to as 19941).
- SEQ ID NO: 476 is the determined cDNA sequence for a fourth splice variant of P775P (referred to as 19937).
- SEQ ID NO: 477 is a first predicted amino acid sequence encoded by the sequence of SEQ ID NO:
- 15 474.
- SEQ ID NO: 478 is a second predicted amino acid sequence encoded by the sequence of SEQ ID NO: 474.
- SEQ ID NO: 479 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: 475.
- 20 SEQ ID NO: 480 is a first predicted amino acid sequence encoded by the sequence of SEQ ID NO: 473.
- SEQ ID NO: 481 is a second predicted amino acid sequence encoded by the sequence of SEQ ID NO: 473.
- SEQ ID NO: 482 is a third predicted amino acid sequence encoded by the sequence of SEQ ID NO:
- 25 473.
- SEQ ID NO: 483 is a fourth predicted amino acid sequence encoded by the sequence of SEQ ID NO: 473.
- SEQ ID NO: 484 is the first 30 amino acids of the *M. tuberculosis* antigen Ra12.
- SEQ ID NO: 485 is the PCR primer AW025.
- 30 SEQ ID NO: 486 is the PCR primer AW003.
- SEQ ID NO: 487 is the PCR primer AW027.
- SEQ ID NO: 488 is the PCR primer AW026.

- SEQ ID NO: 489-501 are peptides employed in epitope mapping studies.
- SEQ ID NO: 502 is the determined cDNA sequence of the complementarity determining region for the anti-P503S monoclonal antibody 20D4.
- SEQ ID NO: 503 is the determined cDNA sequence of the complementarity determining region for the anti-P503S monoclonal antibody JA1.
- SEQ ID NO: 504 & 505 are peptides employed in epitope mapping studies.
- SEQ ID NO: 506 is the determined cDNA sequence of the complementarity determining region for the anti-P703P monoclonal antibody 8H2.
- SEQ ID NO: 507 is the determined cDNA sequence of the complementarity determining region for the anti-P703P monoclonal antibody 7H8.
- SEQ ID NO: 508 is the determined cDNA sequence of the complementarity determining region for the anti-P703P monoclonal antibody 2D4.
- SEQ ID NO: 509-522 are peptides employed in epitope mapping studies.
- SEQ ID NO: 523 is a mature form of P703P used to raise antibodies against P703P. SEQ ID NO: 524 is the putative full-length cDNA sequence of P703P.
- SEQ ID NO: 525 is the predicted amino acid sequence encoded by SEQ ID NO: 524.
- SEQ ID NO: 526 is the full-length cDNA sequence for P790P.
- SEQ ID NO: 527 is the predicted amino acid sequence for P790P.
- SEQ ID NO: 528 & 529 are PCR primers.
- SEQ ID NO: 530 is the cDNA sequence of a splice variant of SEQ ID NO: 366.
- SEQ ID NO: 531 is the cDNA sequence of the open reading frame of SEQ ID NO: 530.
- SEQ ID NO: 532 is the predicted amino acid encoded by the sequence of SEQ ID NO: 531.
- SEQ ID NO: 533 is the DNA sequence of a putative ORF of P775P.
- SEQ ID NO: 534 is the predicted amino acid sequence encoded by SEQ ID NO: 533.
- SEQ ID NO: 535 is a first full-length cDNA sequence for P510S.
- SEQ ID NO: 536 is a second full-length cDNA sequence for P510S.
- SEQ ID NO: 537 is the predicted amino acid sequence encoded by SEQ ID NO: 535.
- SEQ ID NO: 538 is the predicted amino acid sequence encoded by SEQ ID NO: 536.
- SEQ ID NO: 539 is the peptide P501S-370.
- SEQ ID NO: 540 is the peptide P501S-376.
- SEQ ID NO: 541-550 are epitopes of P501S.
- SEQ ID NO: 551 corresponds to amino acids 543-553 of P501S.

DETAILED DESCRIPTION OF THE INVENTION

As noted above, the present invention is generally directed to compositions and methods for the therapy and diagnosis of cancer, such as prostate cancer. The compositions described herein may include prostate-specific polypeptides, polynucleotides encoding such polypeptides, binding agents such as antibodies, antigen presenting cells (APCs) and/or immune system cells (*e.g.*, T cells). Polypeptides of the present invention generally comprise at least a portion (such as an immunogenic portion) of a prostate-specific protein or a variant thereof. A "prostate-specific protein" is a protein that is expressed in normal prostate and/or prostate tumor cells at a level that is at least two fold, and preferably at least five fold, greater than the level of expression in a non-prostate normal tissue, as determined using a representative assay provided herein. Certain prostate-specific proteins are proteins that react detectably (within an immunoassay, such as an ELISA or Western blot) with antisera of a patient afflicted with prostate cancer. Polynucleotides of the subject invention generally comprise a DNA or RNA sequence that encodes all or a portion of such a polypeptide, or that is complementary to such a sequence. Antibodies are generally immune system proteins, or antigen-binding fragments thereof, that are capable of binding to a polypeptide as described above. Antigen presenting cells include dendritic cells, macrophages, monocytes, fibroblasts and B-cells that express a polypeptide as described above. T cells that may be employed within such compositions are generally T cells that are specific for a polypeptide as described above.

The present invention is based on the discovery of human prostate-specific proteins. Sequences of polynucleotides encoding certain prostate-specific proteins, or portions thereof, are provided in SEQ ID NOs:1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382, 384-476, 524, 526, 530, 531, 533, 535 and 536. Sequences of polypeptides comprising at least a portion of a prostate-specific protein are provided in SEQ ID NOs:112-114, 172, 176, 178, 327, 329, 331, 336, 339, 376-380, 383, 477-483, 496, 504, 505, 519, 520, 522, 525, 527, 532, 534 and 537-550.

PROSTATE-SPECIFIC PROTEIN POLYNUCLEOTIDES

Any polynucleotide that encodes a prostate-specific protein or a portion or other variant thereof as described herein is encompassed by the present invention. Preferred

polynucleotides comprise at least 15 consecutive nucleotides, preferably at least 30 consecutive nucleotides and more preferably at least 45 consecutive nucleotides, that encode a portion of a prostate-specific protein. More preferably, a polynucleotide encodes an immunogenic portion of a prostate-specific protein. Polynucleotides complementary to any such sequences are also encompassed by the present invention. Polynucleotides may be single-stranded (coding or antisense) or double-stranded, and may be DNA (genomic, cDNA or synthetic) or RNA molecules. RNA molecules include HnRNA molecules, which contain introns and correspond to a DNA molecule in a one-to-one manner, and mRNA molecules, which do not contain introns. Additional coding or non-coding sequences may, but need not, be present within a polynucleotide of the present invention, and a polynucleotide may, but need not, be linked to other molecules and/or support materials.

Polynucleotides may comprise a native sequence (*i.e.*, an endogenous sequence that encodes a prostate-specific protein or a portion thereof) or may comprise a variant of such a sequence. Polynucleotide variants may contain one or more substitutions, additions, deletions and/or insertions such that the immunogenicity of the encoded polypeptide is not diminished, relative to a native protein. The effect on the immunogenicity of the encoded polypeptide may generally be assessed as described herein. Variants preferably exhibit at least about 70% identity, more preferably at least about 80% identity and most preferably at least about 90% identity to a polynucleotide sequence that encodes a native prostate-specific protein or a portion thereof. The term "variants" also encompasses homologous genes of xenogenic origin.

Two polynucleotide or polypeptide sequences are said to be "identical" if the sequence of nucleotides or amino acids in the two sequences is the same when aligned for maximum correspondence as described below. Comparisons between two sequences are typically performed by comparing the sequences over a comparison window to identify and compare local regions of sequence similarity. A "comparison window" as used herein, refers to a segment of at least about 20 contiguous positions, usually 30 to about 75, 40 to about 50, in which a sequence may be compared to a reference sequence of the same number of contiguous positions after the two sequences are optimally aligned.

Optimal alignment of sequences for comparison may be conducted using the Megalign program in the Lasergene suite of bioinformatics software (DNASTAR, Inc., Madison, WI), using default parameters. This program embodies several alignment schemes described in the following references: Dayhoff, M.O. (1978) A model of evolutionary change in proteins – Matrices

for detecting distant relationships. In Dayhoff, M.O. (ed.) Atlas of Protein Sequence and Structure, National Biomedical Research Foundation, Washington DC Vol. 5, Suppl. 3, pp. 345-358; Hein J. (1990) Unified Approach to Alignment and Phylogenies pp. 626-645 *Methods in Enzymology* vol. 183, Academic Press, Inc., San Diego, CA; Higgins, D.G. and Sharp, P.M. (1989) *CABIOS* 5:151-153; Myers, E.W. and Muller W. (1988) *CABIOS* 4:11-17; Robinson, E.D. (1971) *Comb. Theor* 11:105; Santou, N. Nes, M. (1987) *Mol. Biol. Evol.* 4:406-425; Sneath, P.H.A. and Sokal, R.R. (1973) *Numerical Taxonomy - the Principles and Practice of Numerical Taxonomy*, Freeman Press, San Francisco, CA; Wilbur, W.J. and Lipman, D.J. (1983) *Proc. Natl. Acad., Sci. USA* 80:726-730.

Preferably, the "percentage of sequence identity" is determined by comparing two optimally aligned sequences over a window of comparison of at least 20 positions, wherein the portion of the polynucleotide or polypeptide sequence in the comparison window may comprise additions or deletions (*i.e.*, gaps) of 20 percent or less, usually 5 to 15 percent, or 10 to 12 percent, as compared to the reference sequences (which does not comprise additions or deletions) for optimal alignment of the two sequences. The percentage is calculated by determining the number of positions at which the identical nucleic acid bases or amino acid residue occurs in both sequences to yield the number of matched positions, dividing the number of matched positions by the total number of positions in the reference sequence (*i.e.*, the window size) and multiplying the results by 100 to yield the percentage of sequence identity.

Variants may also, or alternatively, be substantially homologous to a native gene, or a portion or complement thereof. Such polynucleotide variants are capable of hybridizing under moderately stringent conditions to a naturally occurring DNA sequence encoding a native prostate-specific protein (or a complementary sequence). Suitable moderately stringent conditions include prewashing in a solution of 5 X SSC, 0.5% SDS, 1.0 mM EDTA (pH 8.0); hybridizing at 50°C-65°C, 5 X SSC, overnight; followed by washing twice at 65°C for 20 minutes with each of 2X, 0.5X and 0.2X SSC containing 0.1% SDS.

It will be appreciated by those of ordinary skill in the art that, as a result of the degeneracy of the genetic code, there are many nucleotide sequences that encode a polypeptide as described herein. Some of these polynucleotides bear minimal homology to the nucleotide sequence of any native gene. Nonetheless, polynucleotides that vary due to differences in codon usage are specifically contemplated by the present invention. Further, alleles of the genes comprising the polynucleotide sequences provided herein are within the scope of the present invention. Alleles are endogenous genes that are altered as a result of one or more mutations, such

as deletions, additions and/or substitutions of nucleotides. The resulting mRNA and protein may, but need not, have an altered structure or function. Alleles may be identified using standard techniques (such as hybridization, amplification and/or database sequence comparison).

Polynucleotides may be prepared using any of a variety of techniques. For example, a polynucleotide may be identified, as described in more detail below, by screening a microarray of cDNAs for tumor-associated expression (*i.e.*, expression that is at least five fold greater in a prostate-specific than in normal tissue, as determined using a representative assay provided herein). Such screens may be performed using a Synteni microarray (Palo Alto, CA) according to the manufacturer's instructions (and essentially as described by Schena et al., *Proc. Natl. Acad. Sci. USA* 93:10614-10619, 1996 and Heller et al., *Proc. Natl. Acad. Sci. USA* 94:2150-2155, 1997). Alternatively, polypeptides may be amplified from cDNA prepared from cells expressing the proteins described herein, such as prostate-specific cells. Such polynucleotides may be amplified via polymerase chain reaction (PCR). For this approach, sequence-specific primers may be designed based on the sequences provided herein, and may be purchased or synthesized.

An amplified portion may be used to isolate a full length gene from a suitable library (*e.g.*, a prostate-specific cDNA library) using well known techniques. Within such techniques, a library (cDNA or genomic) is screened using one or more polynucleotide probes or primers suitable for amplification. Preferably, a library is size-selected to include larger molecules. Random primed libraries may also be preferred for identifying 5' and upstream regions of genes. Genomic libraries are preferred for obtaining introns and extending 5' sequences.

For hybridization techniques, a partial sequence may be labeled (*e.g.*, by nick-translation or end-labeling with ^{32}P) using well known techniques. A bacterial or bacteriophage library is then screened by hybridizing filters containing denatured bacterial colonies (or lawns containing phage plaques) with the labeled probe (*see* Sambrook et al., *Molecular Cloning: A Laboratory Manual*, Cold Spring Harbor Laboratories, Cold Spring Harbor, NY, 1989). Hybridizing colonies or plaques are selected and expanded, and the DNA is isolated for further analysis. cDNA clones may be analyzed to determine the amount of additional sequence by, for example, PCR using a primer from the partial sequence and a primer from the vector. Restriction maps and partial sequences may be generated to identify one or more overlapping clones. The complete sequence may then be determined using standard techniques, which may involve generating a series of deletion clones. The resulting overlapping sequences are then assembled into

a single contiguous sequence. A full length cDNA molecule can be generated by ligating suitable fragments; using well known techniques.

Alternatively, there are numerous amplification techniques for obtaining a full length coding sequence from a partial cDNA sequence. Within such techniques, amplification is generally performed via PCR. Any of a variety of commercially available kits may be used to perform the amplification step. Primers may be designed using, for example, software well known in the art. Primers are preferably 22-30 nucleotides in length, have a GC content of at least 50% and anneal to the target sequence at temperatures of about 68°C to 72°C. The amplified region may be sequenced as described above, and overlapping sequences assembled into a contiguous sequence.

One such amplification technique is inverse PCR (see Triglia et al., *Nucl. Acids Res.* 16:8186, 1988), which uses restriction enzymes to generate a fragment in the known region of the gene. The fragment is then circularized by intramolecular ligation and used as a template for PCR with divergent primers derived from the known region. Within an alternative approach, sequences adjacent to a partial sequence may be retrieved by amplification with a primer to a linker sequence and a primer specific to a known region. The amplified sequences are typically subjected to a second round of amplification with the same linker primer and a second primer specific to the known region. A variation on this procedure, which employs two primers that initiate extension in opposite directions from the known sequence, is described in WO 96/38591. Another such technique is known as "rapid amplification of cDNA ends" or RACE. This technique involves the use of an internal primer and an external primer, which hybridizes to a polyA region or vector sequence, to identify sequences that are 5' and 3' of a known sequence. Additional techniques include capture PCR (Lagerstrom et al., *PCR Methods Applic.* 1:111-19, 1991) and walking PCR (Parker et al., *Nucl. Acids. Res.* 19:3055-60, 1991). Other methods employing amplification may also be employed to obtain a full length cDNA sequence.

In certain instances, it is possible to obtain a full length cDNA sequence by analysis of sequences provided in an expressed sequence tag (EST) database, such as that available from GenBank. Searches for overlapping ESTs may generally be performed using well known programs (e.g., NCBI BLAST searches), and such ESTs may be used to generate a contiguous full length sequence. Full length DNA sequences may also be obtained by analysis of genomic fragments.

Certain nucleic acid sequences of cDNA molecules encoding at least a portion of a prostate-specific protein are provided in SEQ ID NO:1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382, 384-476, 524, 526, 530, 531, 533, 535 and 536.

Isolation of these polynucleotides is described below. Each of these prostate-specific proteins was overexpressed in prostate tumor tissue.

Polynucleotide variants may generally be prepared by any method known in the art, including chemical synthesis by, for example, solid phase phosphoramidite chemical synthesis.

5 Modifications in a polynucleotide sequence may also be introduced using standard mutagenesis techniques, such as oligonucleotide-directed site-specific mutagenesis (*see* Adelman et al., *DNA* 2:183, 1983). Alternatively, RNA molecules may be generated by *in vitro* or *in vivo* transcription of DNA sequences encoding a prostate-specific protein, or portion thereof, provided that the DNA is incorporated into a vector with a suitable RNA polymerase promoter (such as T7 or SP6). Certain
10 portions may be used to prepare an encoded polypeptide, as described herein. In addition, or alternatively, a portion may be administered to a patient such that the encoded polypeptide is generated *in vivo* (e.g., by transfecting antigen-presenting cells, such as dendritic cells, with a cDNA construct encoding a prostate-specific polypeptide, and administering the transfected cells to the patient).

15 A portion of a sequence complementary to a coding sequence (*i.e.*, an antisense polynucleotide) may also be used as a probe or to modulate gene expression. cDNA constructs that can be transcribed into antisense RNA may also be introduced into cells of tissues to facilitate the production of antisense RNA. An antisense polynucleotide may be used, as described herein, to inhibit expression of a protein. Antisense technology can be used to control gene expression
20 through triple-helix formation, which compromises the ability of the double helix to open sufficiently for the binding of polymerases, transcription factors or regulatory molecules (*see* Gee et al., *In* Huber and Carr, *Molecular and Immunologic Approaches*, Futura Publishing Co. (Mt. Kisco, NY; 1994)). Alternatively, an antisense molecule may be designed to hybridize with a control region of a gene (e.g., promoter, enhancer or transcription initiation site), and block transcription of
25 the gene; or to block translation by inhibiting binding of a transcript to ribosomes.

A portion of a coding sequence, or of a complementary sequence, may also be designed as a probe or primer to detect gene expression. Probes may be labeled with a variety of reporter groups, such as radionuclides and enzymes, and are preferably at least 10 nucleotides in length, more preferably at least 20 nucleotides in length and still more preferably at least 30
30 nucleotides in length. Primers, as noted above, are preferably 22-30 nucleotides in length.

Any polynucleotide may be further modified to increase stability *in vivo*. Possible modifications include, but are not limited to, the addition of flanking sequences at the 5' and/or 3'

ends; the use of phosphorothioate or 2' O-methyl rather than phosphodiesterase linkages in the backbone; and/or the inclusion of nontraditional bases such as inosine, queosine and wybutosine, as well as acetyl- methyl-, thio- and other modified forms of adenine, cytidine, guanine, thymine and uridine.

5 Nucleotide sequences as described herein may be joined to a variety of other nucleotide sequences using established recombinant DNA techniques. For example, a polynucleotide may be cloned into any of a variety of cloning vectors, including plasmids, phagemids, lambda phage derivatives and cosmids. Vectors of particular interest include expression vectors, replication vectors, probe generation vectors and sequencing vectors. In general, a vector
10 will contain an origin of replication functional in at least one organism, convenient restriction endonuclease sites and one or more selectable markers. Other elements will depend upon the desired use, and will be apparent to those of ordinary skill in the art.

Within certain embodiments, polynucleotides may be formulated so as to permit entry into a cell of a mammal, and expression therein. Such formulations are particularly useful for
15 therapeutic purposes, as described below. Those of ordinary skill in the art will appreciate that there are many ways to achieve expression of a polynucleotide in a target cell, and any suitable method may be employed. For example, a polynucleotide may be incorporated into a viral vector such as, but not limited to, adenovirus, adeno-associated virus, retrovirus, or vaccinia or other pox virus (e.g., avian pox virus). The polynucleotides may also be administered as naked plasmid vectors.
20 Techniques for incorporating DNA into such vectors are well known to those of ordinary skill in the art. A retroviral vector may additionally transfer or incorporate a gene for a selectable marker (to aid in the identification or selection of transduced cells) and/or a targeting moiety, such as a gene that encodes a ligand for a receptor on a specific target cell, to render the vector target specific. Targeting may also be accomplished using an antibody, by methods known to those of ordinary
25 skill in the art.

Other formulations for therapeutic purposes include colloidal dispersion systems, such as macromolecule complexes, nanocapsules, microspheres, beads, and lipid-based systems including oil-in-water emulsions, micelles, mixed micelles, and liposomes. A preferred colloidal system for use as a delivery vehicle *in vitro* and *in vivo* is a liposome (i.e., an artificial membrane
30 vesicle). The preparation and use of such systems is well known in the art.

PROSTATE-SPECIFIC POLYPEPTIDES

Within the context of the present invention, polypeptides may comprise at least an immunogenic portion of a prostate-specific protein or a variant thereof, as described herein. As noted above, a "prostate-specific protein" is a protein that is expressed by normal prostate and/or prostate tumor cells. Proteins that are prostate-specific proteins also react detectably within an immunoassay (such as an ELISA) with antisera from a patient with prostate cancer. Polypeptides as described herein may be of any length. Additional sequences derived from the native protein and/or heterologous sequences may be present, and such sequences may (but need not) possess further immunogenic or antigenic properties.

10 An "immunogenic portion," as used herein is a portion of a protein that is recognized (*i.e.*, specifically bound) by a B-cell and/or T-cell surface antigen receptor. Such immunogenic portions generally comprise at least 5 amino acid residues, more preferably at least 10, and still more preferably at least 20 amino acid residues of a prostate-specific protein or a variant thereof. Certain preferred immunogenic portions include peptides in which an N-terminal leader sequence and/or transmembrane domain have been deleted. Other preferred immunogenic portions may contain a small N- and/or C-terminal deletion (*e.g.*, 1-30 amino acids, preferably 5-15 amino acids), relative to the mature protein.

Immunogenic portions may generally be identified using well known techniques, such as those summarized in Paul, *Fundamental Immunology*, 3rd ed., 243-247 (Raven Press, 1993) and references cited therein. Such techniques include screening polypeptides for the ability to react with antigen-specific antibodies, antisera and/or T-cell lines or clones. As used herein, antisera and antibodies are "antigen-specific" if they specifically bind to an antigen (*i.e.*, they react with the protein in an ELISA or other immunoassay, and do not react detectably with unrelated proteins). Such antisera and antibodies may be prepared as described herein, and using well known techniques. An immunogenic portion of a native prostate-specific protein is a portion that reacts with such antisera and/or T-cells at a level that is not substantially less than the reactivity of the full length polypeptide (*e.g.*, in an ELISA and/or T-cell reactivity assay). Such immunogenic portions may react within such assays at a level that is similar to or greater than the reactivity of the full length polypeptide. Such screens may generally be performed using methods well known to those of ordinary skill in the art, such as those described in Harlow and Lane, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, 1988. For example, a polypeptide may be immobilized on a solid support and contacted with patient sera to allow binding of antibodies within the sera to the

immobilized polypeptide. Unbound sera may then be removed and bound antibodies detected using, for example, ¹²⁵I-labeled Protein A.

As noted above, a composition may comprise a variant of a native prostate-specific protein. A polypeptide "variant," as used herein, is a polypeptide that differs from a native prostate-specific protein in one or more substitutions, deletions, additions and/or insertions, such that the immunogenicity of the polypeptide is not substantially diminished. In other words, the ability of a variant to react with antigen-specific antisera may be enhanced or unchanged, relative to the native protein, or may be diminished by less than 50%, and preferably less than 20%, relative to the native protein. Such variants may generally be identified by modifying one of the above polypeptide sequences and evaluating the reactivity of the modified polypeptide with antigen-specific antibodies or antisera as described herein. Preferred variants include those in which one or more portions, such as an N-terminal leader sequence or transmembrane domain, have been removed. Other preferred variants include variants in which a small portion (*e.g.*, 1-30 amino acids, preferably 5-15 amino acids) has been removed from the N- and/or C-terminal of the mature protein. Polypeptide variants preferably exhibit at least about 70%, more preferably at least about 90% and most preferably at least about 95% identity (determined as described above) to the identified polypeptides.

Preferably, a variant contains conservative substitutions. A "conservative substitution" is one in which an amino acid is substituted for another amino acid that has similar properties, such that one skilled in the art of peptide chemistry would expect the secondary structure and hydrophobic nature of the polypeptide to be substantially unchanged. Amino acid substitutions may generally be made on the basis of similarity in polarity, charge, solubility, hydrophobicity, hydrophilicity and/or the amphipathic nature of the residues. For example, negatively charged amino acids include aspartic acid and glutamic acid; positively charged amino acids include lysine and arginine; and amino acids with uncharged polar head groups having similar hydrophilicity values include leucine, isoleucine and valine; glycine and alanine; asparagine and glutamine; and serine, threonine, phenylalanine and tyrosine. Other groups of amino acids that may represent conservative changes include: (1) ala, pro, gly, glu, asp, gln, asn, ser, thr; (2) cys, ser, tyr, thr; (3) val, ile, leu, met, ala, phe; (4) lys, arg, his; and (5) phe, tyr, trp, his. A variant may also, or alternatively, contain nonconservative changes. In a preferred embodiment, variant polypeptides differ from a native sequence by substitution, deletion or addition of five amino acids or fewer. Variants may also (or alternatively) be modified by, for example, the deletion or addition of amino

acids that have minimal influence on the immunogenicity, secondary structure and hydrophobic nature of the polypeptide.

As noted above, polypeptides may comprise a signal (or leader) sequence at the N-terminal end of the protein which co-translationally or post-translationally directs transfer of the protein. The polypeptide may also be conjugated to a linker or other sequence for ease of synthesis, purification or identification of the polypeptide (e.g., poly-His), or to enhance binding of the polypeptide to a solid support. For example, a polypeptide may be conjugated to an immunoglobulin Fc region.

Polypeptides may be prepared using any of a variety of well known techniques. Recombinant polypeptides encoded by DNA sequences as described above may be readily prepared from the DNA sequences using any of a variety of expression vectors known to those of ordinary skill in the art. Expression may be achieved in any appropriate host cell that has been transformed or transfected with an expression vector containing a DNA molecule that encodes a recombinant polypeptide. Suitable host cells include prokaryotes, yeast, higher eukaryotic and plant cells. Preferably, the host cells employed are *E. coli*, yeast or a mammalian cell line such as COS or CHO. Supernatants from suitable host/vector systems which secrete recombinant protein or polypeptide into culture media may be first concentrated using a commercially available filter. Following concentration, the concentrate may be applied to a suitable purification matrix such as an affinity matrix or an ion exchange resin. Finally, one or more reverse phase HPLC steps can be employed to further purify a recombinant polypeptide.

Portions and other variants having fewer than about 100 amino acids, and generally fewer than about 50 amino acids, may also be generated by synthetic means, using techniques well known to those of ordinary skill in the art. For example, such polypeptides may be synthesized using any of the commercially available solid-phase techniques, such as the Merrifield solid-phase synthesis method, where amino acids are sequentially added to a growing amino acid chain. See Merrifield, *J. Am. Chem. Soc.* 85:2149-2146, 1963. Equipment for automated synthesis of polypeptides is commercially available from suppliers such as Perkin Elmer/Applied BioSystems Division (Foster City, CA), and may be operated according to the manufacturer's instructions.

Within certain specific embodiments, a polypeptide may be a fusion protein that comprises multiple polypeptides as described herein, or that comprises at least one polypeptide as described herein and an unrelated sequence, such as a known prostate-specific protein. A fusion partner may, for example, assist in providing T helper epitopes (an immunological fusion partner),

preferably T helper epitopes recognized by humans, or may assist in expressing the protein (an expression enhancer) at higher yields than the native recombinant protein. Certain preferred fusion partners are both immunological and expression enhancing fusion partners. Other fusion partners may be selected so as to increase the solubility of the protein or to enable the protein to be targeted to desired intracellular compartments. Still further fusion partners include affinity tags, which facilitate purification of the protein.

Fusion proteins may generally be prepared using standard techniques, including chemical conjugation. Preferably, a fusion protein is expressed as a recombinant protein, allowing the production of increased levels, relative to a non-fused protein, in an expression system. Briefly, DNA sequences encoding the polypeptide components may be assembled separately, and ligated into an appropriate expression vector. The 3' end of the DNA sequence encoding one polypeptide component is ligated, with or without a peptide linker, to the 5' end of a DNA sequence encoding the second polypeptide component so that the reading frames of the sequences are in phase. This permits translation into a single fusion protein that retains the biological activity of both component polypeptides.

A peptide linker sequence may be employed to separate the first and the second polypeptide components by a distance sufficient to ensure that each polypeptide folds into its secondary and tertiary structures. Such a peptide linker sequence is incorporated into the fusion protein using standard techniques well known in the art. Suitable peptide linker sequences may be chosen based on the following factors: (1) their ability to adopt a flexible extended conformation; (2) their inability to adopt a secondary structure that could interact with functional epitopes on the first and second polypeptides; and (3) the lack of hydrophobic or charged residues that might react with the polypeptide functional epitopes. Preferred peptide linker sequences contain Gly, Asn and Ser residues. Other near neutral amino acids, such as Thr and Ala may also be used in the linker sequence. Amino acid sequences which may be usefully employed as linkers include those disclosed in Maratea et al., *Gene* 40:39-46, 1985; Murphy et al., *Proc. Natl. Acad. Sci. USA* 83:8258-8262, 1986; U.S. Patent No. 4,935,233 and U.S. Patent No. 4,751,180. The linker sequence may generally be from 1 to about 50 amino acids in length. Linker sequences are not required when the first and second polypeptides have non-essential N-terminal amino acid regions that can be used to separate the functional domains and prevent steric interference.

The ligated DNA sequences are operably linked to suitable transcriptional or translational regulatory elements. The regulatory elements responsible for expression of DNA are

located only 5' to the DNA sequence encoding the first polypeptides. Similarly, stop codons required to end translation and transcription termination signals are only present 3' to the DNA sequence encoding the second polypeptide.

Fusion proteins are also provided that comprise a polypeptide of the present invention together with an unrelated immunogenic protein. Preferably the immunogenic protein is capable of eliciting a recall response. Examples of such proteins include tetanus, tuberculosis and hepatitis proteins (*see, for example, Stoute et al. New Engl. J. Med.*, 336:86-91, 1997).

Within preferred embodiments, an immunological fusion partner is derived from protein D, a surface protein of the gram-negative bacterium *Haemophilus influenza B* (WO 91/18926). Preferably, a protein D derivative comprises approximately the first third of the protein (e.g., the first N-terminal 100-110 amino acids), and a protein D derivative may be lipidated. Within certain preferred embodiments, the first 109 residues of a Lipoprotein D fusion partner is included on the N-terminus to provide the polypeptide with additional exogenous T-cell epitopes and to increase the expression level in *E. coli* (thus functioning as an expression enhancer). The lipid tail ensures optimal presentation of the antigen to antigen presenting cells. Other fusion partners include the non-structural protein from influenzae virus, NS1 (hemagglutinin). Typically, the N-terminal 81 amino acids are used, although different fragments that include T-helper epitopes may be used.

In another embodiment, the immunological fusion partner is the protein known as LYTA, or a portion thereof (preferably a C-terminal portion). LYTA is derived from *Streptococcus pneumoniae*, which synthesizes an N-acetyl-L-alanine amidase known as amidase LYTA (encoded by the *LytA* gene; *Gene* 43:265-292, 1986). LYTA is an autolysin that specifically degrades certain bonds in the peptidoglycan backbone. The C-terminal domain of the LYTA protein is responsible for the affinity to the choline or to some choline analogues such as DEAE. This property has been exploited for the development of *E. coli* C-LYTA expressing plasmids useful for expression of fusion proteins. Purification of hybrid proteins containing the C-LYTA fragment at the amino terminus has been described (*see Biotechnology* 10:795-798, 1992). Within a preferred embodiment, a repeat portion of LYTA may be incorporated into a fusion protein. A repeat portion is found in the C-terminal region starting at residue 178. A particularly preferred repeat portion incorporates residues 188-305.

In general, polypeptides (including fusion proteins) and polynucleotides as described herein are isolated. An "isolated" polypeptide or polynucleotide is one that is removed from its

original environment. For example, a naturally-occurring protein is isolated if it is separated from some or all of the coexisting materials in the natural system. Preferably, such polypeptides are at least about 90% pure, more preferably at least about 95% pure and most preferably at least about 99% pure. A polynucleotide is considered to be isolated if, for example, it is cloned into a vector
5 that is not a part of the natural environment.

BINDING AGENTS

The present invention further provides agents, such as antibodies and antigen-binding fragments thereof, that specifically bind to a prostate-specific protein. As used herein, an
10 antibody, or antigen-binding fragment thereof, is said to "specifically bind" to a prostate-specific protein if it reacts at a detectable level (within, for example, an ELISA) with a prostate-specific protein, and does not react detectably with unrelated proteins under similar conditions. As used herein, "binding" refers to a noncovalent association between two separate molecules such that a complex is formed. The ability to bind may be evaluated by, for example, determining a binding
15 constant for the formation of the complex. The binding constant is the value obtained when the concentration of the complex is divided by the product of the component concentrations. In general, two compounds are said to "bind," in the context of the present invention, when the binding constant for complex formation exceeds about 10^3 L/mol. The binding constant may be determined using methods well known in the art.

20 Binding agents may be further capable of differentiating between patients with and without a cancer, such as prostate cancer, using the representative assays provided herein. In other words, antibodies or other binding agents that bind to a prostate-specific protein will generate a signal indicating the presence of a cancer in at least about 20% of patients with the disease, and will generate a negative signal indicating the absence of the disease in at least about 90% of individuals
25 without the cancer. To determine whether a binding agent satisfies this requirement, biological samples (e.g., blood, sera, urine and/or tumor biopsies) from patients with and without a cancer (as determined using standard clinical tests) may be assayed as described herein for the presence of polypeptides that bind to the binding agent. It will be apparent that a statistically significant number of samples with and without the disease should be assayed. Each binding agent should satisfy the
30 above criteria; however, those of ordinary skill in the art will recognize that binding agents may be used in combination to improve sensitivity.

Any agent that satisfies the above requirements may be a binding agent. For example, a binding agent may be a ribosome, with or without a peptide component, an RNA molecule or a polypeptide. In a preferred embodiment, a binding agent is an antibody or an antigen-binding fragment thereof. Most preferably, antibodies employed in the inventive methods have the ability to induce lysis of tumor cells by activation of complement and mediation of antibody-dependent cellular cytotoxicity (ADCC). Antibodies of different classes and subclasses differ in these properties. For example, mouse antibodies of the IgG2a and IgG3 classes are capable of activating serum complement upon binding to target cells which express the antigen against which the antibodies were raised, and can mediate ADCC.

Antibodies may be prepared by any of a variety of techniques known to those of ordinary skill in the art. See, e.g., Harlow and Lane, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, 1988. In general, antibodies can be produced by cell culture techniques, including the generation of monoclonal antibodies as described herein, or via transfection of antibody genes into suitable bacterial or mammalian cell hosts, in order to allow for the production of recombinant antibodies. In one technique, an immunogen comprising the polypeptide is initially injected into any of a wide variety of mammals (e.g., mice, rats, rabbits, sheep or goats). In this step, the polypeptides of this invention may serve as the immunogen without modification. Alternatively, particularly for relatively short polypeptides, a superior immune response may be elicited if the polypeptide is joined to a carrier protein, such as bovine serum albumin or keyhole limpet hemocyanin. The immunogen is injected into the animal host, preferably according to a predetermined schedule incorporating one or more booster immunizations, and the animals are bled periodically. Polyclonal antibodies specific for the polypeptide may then be purified from such antisera by, for example, affinity chromatography using the polypeptide coupled to a suitable solid support.

Monoclonal antibodies specific for an antigenic polypeptide of interest may be prepared, for example, using the technique of Kohler and Milstein, *Eur. J. Immunol.* 6:511-519, 1976, and improvements thereto. Briefly, these methods involve the preparation of immortal cell lines capable of producing antibodies having the desired specificity (i.e., reactivity with the polypeptide of interest). Such cell lines may be produced, for example, from spleen cells obtained from an animal immunized as described above. The spleen cells are then immortalized by, for example, fusion with a myeloma cell fusion partner, preferably one that is syngeneic with the immunized animal. A variety of fusion techniques may be employed. For example, the spleen cells

and myeloma cells may be combined with a nonionic detergent for a few minutes and then plated at low density on a selective medium that supports the growth of hybrid cells, but not myeloma cells. A preferred selection technique uses HAT (hypoxanthine, aminopterin, thymidine) selection. After a sufficient time, usually about 1 to 2 weeks, colonies of hybrids are observed. Single colonies are
5 selected and their culture supernatants tested for binding activity against the polypeptide. Hybridomas having high reactivity and specificity are preferred.

Monoclonal antibodies may be isolated from the supernatants of growing hybridoma colonies. In addition, various techniques may be employed to enhance the yield, such as injection of the hybridoma cell line into the peritoneal cavity of a suitable vertebrate host, such as a mouse.
10 Monoclonal antibodies may then be harvested from the ascites fluid or the blood. Contaminants may be removed from the antibodies by conventional techniques, such as chromatography, gel filtration, precipitation, and extraction. The polypeptides of this invention may be used in the purification process in, for example, an affinity chromatography step.

The preparation of mouse and rabbit monoclonal antibodies that specifically bind to
15 polypeptides of the present invention is described in detail below. However, the antibodies of the present invention are not limited to those derived from mice. Human antibodies may also be employed in the inventive methods and may prove to be preferable. Such antibodies can be obtained using human hybridomas as described by Cote *et al.* (Monoclonal Antibodies and Cancer Therapy, Alan R. Lisa, p. 77, 1985). The present invention also encompasses antibodies made by
20 recombinant means such as chimeric antibodies, wherein the variable region and constant region are derived from different species, and CDR-grafted antibodies, wherein the complementarity determining region is derived from a different species, as described in US Patents 4,816,567 and 5,225,539. Chimeric antibodies may be prepared by splicing genes for a mouse antibody molecule having a desired antigen specificity together with genes for a human antibody molecule having the
25 desired biological activity, such as activation of human complement and mediation of ADCC (Morrison *et al. Proc. Natl. Acad. Sci. USA* 81:6851, 1984; Neuberger *et al. Nature* 312:604, 1984; Takeda *et al. Nature* 314:452, 1985).

Within certain embodiments, the use of antigen-binding fragments of antibodies may be preferred. Such fragments include Fab fragments, which may be prepared using standard
30 techniques. Briefly, immunoglobulins may be purified from rabbit serum by affinity chromatography on Protein A bead columns (Harlow and Lane, *Antibodies: A Laboratory Manual*,

Cold Spring Harbor Laboratory, 1988) and digested by papain to yield Fab and Fc fragments. The Fab and Fc fragments may be separated by affinity chromatography on protein A bead columns.

Monoclonal antibodies of the present invention may be coupled to one or more therapeutic agents. Suitable agents in this regard include radionuclides, differentiation inducers, drugs, toxins, and derivatives thereof. Preferred radionuclides include ^{90}Y , ^{123}I , ^{125}I , ^{131}I , ^{186}Re , ^{188}Re , ^{211}At , and ^{212}Bi . Preferred drugs include methotrexate, and pyrimidine and purine analogs. Preferred differentiation inducers include phorbol esters and butyric acid. Preferred toxins include ricin, abrin, diphtheria toxin, cholera toxin, gelonin, *Pseudomonas* exotoxin, *Shigella* toxin, and pokeweed antiviral protein.

10 A therapeutic agent may be coupled (*e.g.*, covalently bonded) to a suitable monoclonal antibody either directly or indirectly (*e.g.*, via a linker group). A direct reaction between an agent and an antibody is possible when each possesses a substituent capable of reacting with the other. For example, a nucleophilic group, such as an amino or sulfhydryl group, on one may be capable of reacting with a carbonyl-containing group, such as an anhydride or an acid
15 halide, or with an alkyl group containing a good leaving group (*e.g.*, a halide) on the other.

Alternatively, it may be desirable to couple a therapeutic agent and an antibody via a linker group. A linker group can function as a spacer to distance an antibody from an agent in order to avoid interference with binding capabilities. A linker group can also serve to increase the chemical reactivity of a substituent on an agent or an antibody, and thus increase the coupling
20 efficiency. An increase in chemical reactivity may also facilitate the use of agents, or functional groups on agents, which otherwise would not be possible.

It will be evident to those skilled in the art that a variety of bifunctional or polyfunctional reagents, both homo- and hetero-functional (such as those described in the catalog of the Pierce Chemical Co., Rockford, IL), may be employed as the linker group. Coupling may be
25 effected, for example, through amino groups, carboxyl groups, sulfhydryl groups or oxidized carbohydrate residues. There are numerous references describing such methodology, *e.g.*, U.S. Patent No. 4,671,958, to Rodwell et al.

Where a therapeutic agent is more potent when free from the antibody portion of the immunoconjugates of the present invention, it may be desirable to use a linker group which is
30 cleavable during or upon internalization into a cell. A number of different cleavable linker groups have been described. The mechanisms for the intracellular release of an agent from these linker groups include cleavage by reduction of a disulfide bond (*e.g.*, U.S. Patent No. 4,489,710, to

Spitler), by irradiation of a photolabile bond (*e.g.*, U.S. Patent No. 4,625,014, to Senter et al.), by hydrolysis of derivatized amino acid side chains (*e.g.*, U.S. Patent No. 4,638,045, to Kohn et al.), by serum complement-mediated hydrolysis (*e.g.*, U.S. Patent No. 4,671,958, to Rodwell et al.), and acid-catalyzed hydrolysis (*e.g.*, U.S. Patent No. 4,569,789, to Blattler et al.).

5 It may be desirable to couple more than one agent to an antibody. In one embodiment, multiple molecules of an agent are coupled to one antibody molecule. In another embodiment, more than one type of agent may be coupled to one antibody. Regardless of the particular embodiment, immunoconjugates with more than one agent may be prepared in a variety of ways. For example, more than one agent may be coupled directly to an antibody molecule, or
10 linkers which provide multiple sites for attachment can be used. Alternatively, a carrier can be used.

 A carrier may bear the agents in a variety of ways, including covalent bonding either directly or via a linker group. Suitable carriers include proteins such as albumins (*e.g.*, U.S. Patent No. 4,507,234, to Kato et al.), peptides and polysaccharides such as aminodextran (*e.g.*, U.S. Patent
15 No. 4,699,784, to Shih et al.). A carrier may also bear an agent by noncovalent bonding or by encapsulation, such as within a liposome vesicle (*e.g.*, U.S. Patent Nos. 4,429,008 and 4,873,088). Carriers specific for radionuclide agents include radiohalogenated small molecules and chelating compounds. For example, U.S. Patent No. 4,735,792 discloses representative radiohalogenated small molecules and their synthesis. A radionuclide chelate may be formed from chelating
20 compounds that include those containing nitrogen and sulfur atoms as the donor atoms for binding the metal, or metal oxide, radionuclide. For example, U.S. Patent No. 4,673,562, to Davison et al. discloses representative chelating compounds and their synthesis.

 A variety of routes of administration for the antibodies and immunoconjugates may be used. Typically, administration will be intravenous, intramuscular, subcutaneous or in the bed of
25 a resected tumor. It will be evident that the precise dose of the antibody/immunoconjugate will vary depending upon the antibody used, the antigen density on the tumor, and the rate of clearance of the antibody.

T CELLS

30 Immunotherapeutic compositions may also, or alternatively, comprise T cells specific for a prostate-specific protein. Such cells may generally be prepared *in vitro* or *ex vivo*, using standard procedures. For example, T cells may be isolated from bone marrow, peripheral

blood, or a fraction of bone marrow or peripheral blood of a patient, using a commercially available cell separation system, such as the ISOLEX™ system, available from Nexell Therapeutics Inc., Irvine, CA (see also U.S. Patent No. 5,240,856; U.S. Patent No. 5,215,926; WO 89/06280; WO 91/16116 and WO 92/07243). Alternatively, T cells may be derived from related or unrelated
5 humans, non-human mammals, cell lines or cultures.

T cells may be stimulated with a prostate-specific polypeptide, polynucleotide encoding a prostate-specific polypeptide and/or an antigen presenting cell (APC) that expresses such a polypeptide. Such stimulation is performed under conditions and for a time sufficient to permit the generation of T cells that are specific for the polypeptide. Preferably, a prostate-specific
10 polypeptide or polynucleotide is present within a delivery vehicle, such as a microsphere, to facilitate the generation of specific T cells.

T cells are considered to be specific for a prostate-specific polypeptide if the T cells specifically proliferate, secrete cytokines or kill target cells coated with the polypeptide or expressing a gene encoding the polypeptide. T cell specificity may be evaluated using any of a
15 variety of standard techniques. For example, within a chromium release assay or proliferation assay, a stimulation index of more than two fold increase in lysis and/or proliferation, compared to negative controls, indicates T cell specificity. Such assays may be performed, for example, as described in Chen et al., *Cancer Res.* 54:1065-1070, 1994. Alternatively, detection of the proliferation of T cells may be accomplished by a variety of known techniques. For example, T cell
20 proliferation can be detected by measuring an increased rate of DNA synthesis (e.g., by pulse-labeling cultures of T cells with tritiated thymidine and measuring the amount of tritiated thymidine incorporated into DNA). Contact with a prostate-specific polypeptide (100 ng/ml - 100 µg/ml, preferably 200 ng/ml - 25 µg/ml) for 3 - 7 days should result in at least a two fold increase in proliferation of the T cells. Contact as described above for 2-3 hours should result in activation of
25 the T cells, as measured using standard cytokine assays in which a two fold increase in the level of cytokine release (e.g., TNF or IFN-γ) is indicative of T cell activation (see Coligan et al., *Current Protocols in Immunology*, vol. 1, Wiley Interscience (Greene 1998)). T cells that have been activated in response to a prostate-specific polypeptide, polynucleotide or polypeptide-expressing APC may be CD4⁺ and/or CD8⁺. Prostate-specific protein-specific T cells may be expanded using
30 standard techniques. Within preferred embodiments, the T cells are derived from either a patient or a related, or unrelated, donor and are administered to the patient following stimulation and expansion.

For therapeutic purposes, CD4⁺ or CD8⁺ T cells that proliferate in response to a prostate-specific polypeptide, polynucleotide or APC can be expanded in number either *in vitro* or *in vivo*. Proliferation of such T cells *in vitro* may be accomplished in a variety of ways. For example, the T cells can be re-exposed to a prostate-specific polypeptide, or a short peptide
5 corresponding to an immunogenic portion of such a polypeptide, with or without the addition of T cell growth factors, such as interleukin-2, and/or stimulator cells that synthesize a prostate-specific polypeptide. Alternatively, one or more T cells that proliferate in the presence of a prostate-specific protein can be expanded in number by cloning. Methods for cloning cells are well known in the art, and include limiting dilution.

16 PHARMACEUTICAL COMPOSITIONS AND VACCINES

Within certain aspects, polypeptides, polynucleotides, T cells and/or binding agents disclosed herein may be incorporated into pharmaceutical compositions or immunogenic compositions (*i.e.*, vaccines). Pharmaceutical compositions comprise one or more such compounds
15 and a physiologically acceptable carrier. Vaccines may comprise one or more such compounds and an immunostimulant. An immunostimulant may be any substance that enhances an immune response to an exogenous antigen. Examples of immunostimulants include adjuvants, biodegradable microspheres (*e.g.*, polylactic galactide) and liposomes (into which the compound is incorporated; *see e.g.*, Fullerton, U.S. Patent No. 4,235,877). Vaccine preparation is generally
20 described in, for example, M.F. Powell and M.J. Newman, eds., "Vaccine Design (the subunit and adjuvant approach)," Plenum Press (NY, 1995). Pharmaceutical compositions and vaccines within the scope of the present invention may also contain other compounds, which may be biologically active or inactive. For example, one or more immunogenic portions of other tumor antigens may be present, either incorporated into a fusion polypeptide or as a separate compound, within the
25 composition or vaccine.

A pharmaceutical composition or vaccine may contain DNA encoding one or more of the polypeptides as described above, such that the polypeptide is generated *in situ*. As noted above, the DNA may be present within any of a variety of delivery systems known to those of ordinary skill in the art, including nucleic acid expression systems, bacteria and viral expression
30 systems. Numerous gene delivery techniques are well known in the art, such as those described by Rolland, *Crit. Rev. Therap. Drug Carrier Systems* 15:143-198, 1998, and references cited therein. Appropriate nucleic acid expression systems contain the necessary DNA sequences for expression

in the patient (such as a suitable promoter and terminating signal). Bacterial delivery systems involve the administration of a bacterium (such as *Bacillus-Calmette-Guerrin*) that expresses an immunogenic portion of the polypeptide on its cell surface or secretes such an epitope. In a preferred embodiment, the DNA may be introduced using a viral expression system (*e.g.*, vaccinia or other pox virus, retrovirus, or adenovirus), which may involve the use of a non-pathogenic (defective), replication competent virus. Suitable systems are disclosed, for example, in Fisher-Hoch et al., *Proc. Natl. Acad. Sci. USA* 86:317-321, 1989; Flexner et al., *Ann. N.Y. Acad. Sci.* 569:86-103, 1989; Flexner et al., *Vaccine* 8:17-21, 1990; U.S. Patent Nos. 4,603,112, 4,769,330, and 5,017,487; WO 89/01973; U.S. Patent No. 4,777,127; GB 2,200,651; EP 0,345,242; WO 91/02805; Berkner, *Biotechniques* 6:616-627, 1988; Rosenfeld et al., *Science* 252:431-434, 1991; Kolls et al., *Proc. Natl. Acad. Sci. USA* 91:215-219, 1994; Kass-Eisler et al., *Proc. Natl. Acad. Sci. USA* 90:11498-11502, 1993; Guzman et al., *Circulation* 88:2838-2848, 1993; and Guzman et al., *Cir. Res.* 73:1202-1207, 1993. Techniques for incorporating DNA into such expression systems are well known to those of ordinary skill in the art. The DNA may also be "naked," as described, for example, in Ulmer et al., *Science* 259:1745-1749, 1993 and reviewed by Cohen, *Science* 259:1691-1692, 1993. The uptake of naked DNA may be increased by coating the DNA onto biodegradable beads, which are efficiently transported into the cells.

While any suitable carrier known to those of ordinary skill in the art may be employed in the pharmaceutical compositions of this invention, the type of carrier will vary depending on the mode of administration. Compositions of the present invention may be formulated for any appropriate manner of administration, including for example, topical, oral, nasal, intravenous, intracranial, intraperitoneal, subcutaneous or intramuscular administration. For parenteral administration, such as subcutaneous injection, the carrier preferably comprises water, saline, alcohol, a fat, a wax or a buffer. For oral administration, any of the above carriers or a solid carrier, such as mannitol, lactose, starch, magnesium stearate, sodium saccharine, talcum, cellulose, glucose, sucrose, and magnesium carbonate, may be employed. Biodegradable microspheres (*e.g.*, polylactate polyglycolate) may also be employed as carriers for the pharmaceutical compositions of this invention. Suitable biodegradable microspheres are disclosed, for example, in U.S. Patent Nos. 4,897,268 and 5,075,109.

Such compositions may also comprise buffers (*e.g.*, neutral buffered saline or phosphate buffered saline), carbohydrates (*e.g.*, glucose, mannose, sucrose or dextrans), mannitol, proteins, polypeptides or amino acids such as glycine, antioxidants, chelating agents such as EDTA

or glutathione, adjuvants (e.g., aluminum hydroxide) and/or preservatives. Alternatively, compositions of the present invention may be formulated as a lyophilizate. Compounds may also be encapsulated within liposomes using well known technology.

Any of a variety of immunostimulants may be employed in the vaccines of this invention. For example, an adjuvant may be included. Most adjuvants contain a substance designed to protect the antigen from rapid catabolism, such as aluminum hydroxide or mineral oil, and a stimulator of immune responses, such as lipid A, *Bordetella pertussis* or *Mycobacterium tuberculosis* derived proteins. Suitable adjuvants are commercially available as, for example, Freund's Incomplete Adjuvant and Complete Adjuvant (Difco Laboratories, Detroit, MI); Merck Adjuvant 65 (Merck and Company, Inc., Rahway, NJ); aluminum salts such as aluminum hydroxide gel (alum) or aluminum phosphate; salts of calcium, iron or zinc; an insoluble suspension of acylated tyrosine; acylated sugars; cationically or anionically derivatized polysaccharides; polyphosphazenes; biodegradable microspheres; monophosphoryl lipid A and quil A. Cytokines, such as GM-CSF or interleukin-2, -7, or -12, may also be used as adjuvants.

Within the vaccines provided herein, the adjuvant composition is preferably designed to induce an immune response predominantly of the Th1 type. High levels of Th1-type cytokines (e.g., IFN- γ , TNF α , IL-2 and IL-12) tend to favor the induction of cell mediated immune responses to an administered antigen. In contrast, high levels of Th2-type cytokines (e.g., IL-4, IL-5, IL-6 and IL-10) tend to favor the induction of humoral immune responses. Following application of a vaccine as provided herein, a patient will support an immune response that includes Th1- and Th2-type responses. Within a preferred embodiment, in which a response is predominantly Th1-type, the level of Th1-type cytokines will increase to a greater extent than the level of Th2-type cytokines. The levels of these cytokines may be readily assessed using standard assays. For a review of the families of cytokines, see Mosmann and Coffman, *Ann. Rev. Immunol.* 7:145-173, 1989.

Preferred adjuvants for use in eliciting a predominantly Th1-type response include, for example, a combination of monophosphoryl lipid A, preferably 3-de-O-acylated monophosphoryl lipid A (3D-MPL), together with an aluminum salt. MPL adjuvants are available from Ribi ImmunoChem Research Inc. (Hamilton, MT; see US Patent Nos. 4,436,727; 4,877,611; 4,866,034 and 4,912,094). CpG-containing oligonucleotides (in which the CpG dinucleotide is unmethylated) also induce a predominantly Th1 response. Such oligonucleotides are well known and are described, for example, in WO 96/02555. Another preferred adjuvant is a saponin, preferably QS21, which may be used alone or in combination with other adjuvants. For example,

an enhanced system involves the combination of a monophosphoryl lipid A and saponin derivative, such as the combination of QS21 and 3D-MPL as described in WO 94/00153, or a less reactogenic composition where the QS21 is quenched with cholesterol, as described in WO 96/33739. Other preferred formulations comprises an oil-in-water emulsion and tocopherol. A particularly potent
5 adjuvant formulation involving QS21, 3D-MPL and tocopherol in an oil-in-water emulsion is described in WO 95/17210. Any vaccine provided herein may be prepared using well known methods that result in a combination of antigen, immune response enhancer and a suitable carrier or excipient.

The compositions described herein may be administered as part of a sustained release
10 formulation (*i.e.*, a formulation such as a capsule, sponge or gel (composed of polysaccharides for example) that effects a slow release of compound following administration). Such formulations may generally be prepared using well known technology and administered by, for example, oral, rectal or subcutaneous implantation, or by implantation at the desired target site. Sustained-release formulations may contain a polypeptide, polynucleotide or antibody dispersed in a carrier matrix
15 and/or contained within a reservoir surrounded by a rate controlling membrane. Carriers for use within such formulations are biocompatible, and may also be biodegradable; preferably the formulation provides a relatively constant level of active component release. The amount of active compound contained within a sustained release formulation depends upon the site of implantation, the rate and expected duration of release and the nature of the condition to be treated or prevented.

Any of a variety of delivery vehicles may be employed within pharmaceutical
20 compositions and vaccines to facilitate production of an antigen-specific immune response that targets tumor cells. Delivery vehicles include antigen presenting cells (APCs), such as dendritic cells, macrophages, B cells, monocytes and other cells that may be engineered to be efficient APCs. Such cells may, but need not, be genetically modified to increase the capacity for presenting the
25 antigen, to improve activation and/or maintenance of the T cell response, to have anti-tumor effects *per se* and/or to be immunologically compatible with the receiver (*i.e.*, matched HLA haplotype). APCs may generally be isolated from any of a variety of biological fluids and organs, including tumor and peritumoral tissues, and may be autologous, allogeneic, syngeneic or xenogeneic cells.

Certain preferred embodiments of the present invention use dendritic cells or
30 progenitors thereof as antigen-presenting cells. Dendritic cells are highly potent APCs (Banchereau and Steinman, *Nature* 392:245-251, 1998) and have been shown to be effective as a physiological adjuvant for eliciting prophylactic or therapeutic antitumor immunity (*see* Timmerman and Levy,

Ann. Rev. Med. 50:507-529, 1999). In general, dendritic cells may be identified based on their typical shape (stellate *in situ*, with marked cytoplasmic processes (dendrites) visible *in vitro*), their ability to take-up, process and present antigens with high efficiency, and their ability to activate naïve T cell responses. Dendritic cells may, of course, be engineered to express specific cell-surface
5 receptors or ligands that are not commonly found on dendritic cells *in vivo* or *ex vivo*, and such modified dendritic cells are contemplated by the present invention. As an alternative to dendritic cells, secreted vesicles antigen-loaded dendritic cells (called exosomes) may be used within a vaccine (see Zitvogel et al., *Nature Med.* 4:594-600, 1998).

Dendritic cells and progenitors may be obtained from peripheral blood, bone
10 marrow, tumor-infiltrating cells, peritumoral tissues-infiltrating cells, lymph nodes, spleen, skin, umbilical cord blood or any other suitable tissue or fluid. For example, dendritic cells may be differentiated *ex vivo* by adding a combination of cytokines such as GM-CSF, IL-4, IL-13 and/or TNF α to cultures of monocytes harvested from peripheral blood. Alternatively, CD34 positive cells harvested from peripheral blood, umbilical cord blood or bone marrow may be differentiated into
15 dendritic cells by adding to the culture medium combinations of GM-CSF, IL-3, TNF α , CD40 ligand, LPS, flt3 ligand and/or other compound(s) that induce differentiation, maturation and proliferation of dendritic cells.

Dendritic cells are conveniently categorized as "immature" and "mature" cells, which allows a simple way to discriminate between two well characterized phenotypes. However, this
20 nomenclature should not be construed to exclude all possible intermediate stages of differentiation. Immature dendritic cells are characterized as APC with a high capacity for antigen uptake and processing, which correlates with the high expression of Fc γ receptor and mannose receptor. The mature phenotype is typically characterized by a lower expression of these markers, but a high expression of cell surface molecules responsible for T cell activation such as class I and class II
25 MHC, adhesion molecules (*e.g.*, CD54 and CD11) and costimulatory molecules (*e.g.*, CD40, CD80, CD86 and 4-1BB).

APCs may generally be transfected with a polynucleotide encoding a prostate-specific protein (or portion or other variant thereof) such that the prostate-specific polypeptide, or an immunogenic portion thereof, is expressed on the cell surface. Such transfection may take place *ex*
30 *vivo*, and a composition or vaccine comprising such transfected cells may then be used for therapeutic purposes, as described herein. Alternatively, a gene delivery vehicle that targets a dendritic or other antigen presenting cell may be administered to a patient, resulting in transfection

that occurs *in vivo*. *In vivo* and *ex vivo* transfection of dendritic cells, for example, may generally be performed using any methods known in the art, such as those described in WO 97/24447, or the gene gun approach described by Mahvi et al., *Immunology and cell Biology* 75:456-460, 1997. Antigen loading of dendritic cells may be achieved by incubating dendritic cells or progenitor cells
5 with the prostate-specific polypeptide, DNA (naked or within a plasmid vector) or RNA; or with antigen-expressing recombinant bacterium or viruses (*e.g.*, vaccinia, fowlpox, adenovirus or lentivirus vectors). Prior to loading, the polypeptide may be covalently conjugated to an immunological partner that provides T cell help (*e.g.*, a carrier molecule). Alternatively, a dendritic cell may be pulsed with a non-conjugated immunological partner, separately or in the presence of
10 the polypeptide.

CANCER THERAPY

In further aspects of the present invention, the compositions described herein may be used for immunotherapy of cancer, such as prostate cancer. Within such methods, pharmaceutical
15 compositions and vaccines are typically administered to a patient. As used herein, a "patient" refers to any warm-blooded animal, preferably a human. A patient may or may not be afflicted with cancer. Accordingly, the above pharmaceutical compositions and vaccines may be used to prevent the development of a cancer or to treat a patient afflicted with a cancer. A cancer may be diagnosed using criteria generally accepted in the art, including the presence of a malignant tumor.
20 Pharmaceutical compositions and vaccines may be administered either prior to or following surgical removal of primary tumors and/or treatment such as administration of radiotherapy or conventional chemotherapeutic drugs.

Within certain embodiments, immunotherapy may be active immunotherapy, in which treatment relies on the *in vivo* stimulation of the endogenous host immune system to react
25 against tumors with the administration of immune response-modifying agents (such as polypeptides and polynucleotides disclosed herein).

Within other embodiments, immunotherapy may be passive immunotherapy, in which treatment involves the delivery of agents with established tumor-immune reactivity (such as effector cells or antibodies) that can directly or indirectly mediate antitumor effects and does not
30 necessarily depend on an intact host immune system. Examples of effector cells include T cells as discussed above, T lymphocytes (such as CD8⁺ cytotoxic T lymphocytes and CD4⁺ T-helper tumor-infiltrating lymphocytes), killer cells (such as Natural Killer cells and lymphokine-activated killer

cells), B cells and antigen-presenting cells (such as dendritic cells and macrophages) expressing a polypeptide provided herein. T cell receptors and antibody receptors specific for the polypeptides recited herein may be cloned, expressed and transferred into other vectors or effector cells for adoptive immunotherapy. The polypeptides provided herein may also be used to generate
5 antibodies or anti-idiotypic antibodies (as described above and in U.S. Patent No. 4,918,164) for passive immunotherapy.

Effector cells may generally be obtained in sufficient quantities for adoptive immunotherapy by growth *in vitro*, as described herein. Culture conditions for expanding single antigen-specific effector cells to several billion in number with retention of antigen recognition *in*
10 *vivo* are well known in the art. Such *in vitro* culture conditions typically use intermittent stimulation with antigen, often in the presence of cytokines (such as IL-2) and non-dividing feeder cells. As noted above, immunoreactive polypeptides as provided herein may be used to rapidly expand antigen-specific T cell cultures in order to generate a sufficient number of cells for immunotherapy. In particular, antigen-presenting cells, such as dendritic, macrophage, monocyte,
15 fibroblast or B cells, may be pulsed with immunoreactive polypeptides or transfected with one or more polynucleotides using standard techniques well known in the art. For example, antigen-presenting cells can be transfected with a polynucleotide having a promoter appropriate for increasing expression in a recombinant virus or other expression system. Cultured effector cells for use in therapy must be able to grow and distribute widely, and to survive long term *in vivo*. Studies
20 have shown that cultured effector cells can be induced to grow *in vivo* and to survive long term in substantial numbers by repeated stimulation with antigen supplemented with IL-2 (*see*, for example, Cheever et al., *Immunological Reviews* 157:177, 1997).

Alternatively, a vector expressing a polypeptide recited herein may be introduced into antigen presenting cells taken from a patient and clonally propagated *ex vivo* for transplant back
25 into the same patient. Transfected cells may be reintroduced into the patient using any means known in the art, preferably in sterile form by intravenous, intracavitary, intraperitoneal or intratumor administration.

Routes and frequency of administration of the therapeutic compositions disclosed herein, as well as dosage, will vary from individual to individual, and may be readily established
30 using standard techniques. In general, the pharmaceutical compositions and vaccines may be administered by injection (*e.g.*, intracutaneous, intramuscular, intravenous or subcutaneous), intranasally (*e.g.*, by aspiration) or orally. Preferably, between 1 and 10 doses may be administered

over a 52 week period. Preferably, 6 doses are administered, at intervals of 1 month, and booster vaccinations may be given periodically thereafter. Alternate protocols may be appropriate for individual patients. A suitable dose is an amount of a compound that, when administered as described above, is capable of promoting an anti-tumor immune response, and is at least 10-50%
5 above the basal (*i.e.*, untreated) level. Such response can be monitored by measuring the anti-tumor antibodies in a patient or by vaccine-dependent generation of cytolytic effector cells capable of killing the patient's tumor cells *in vitro*. Such vaccines should also be capable of causing an immune response that leads to an improved clinical outcome (*e.g.*, more frequent remissions, complete or partial or longer disease-free survival) in vaccinated patients as compared to non-
10 vaccinated patients. In general, for pharmaceutical compositions and vaccines comprising one or more polypeptides, the amount of each polypeptide present in a dose ranges from about 25 µg to 5 mg per kg of host. Suitable dose sizes will vary with the size of the patient, but will typically range from about 0.1 mL to about 5 mL.

In general, an appropriate dosage and treatment regimen provides the active
15 compound(s) in an amount sufficient to provide therapeutic and/or prophylactic benefit. Such a response can be monitored by establishing an improved clinical outcome (*e.g.*, more frequent remissions, complete or partial, or longer disease-free survival) in treated patients as compared to non-treated patients. Increases in preexisting immune responses to a prostate-specific protein generally correlate with an improved clinical outcome. Such immune responses may generally be
20 evaluated using standard proliferation, cytotoxicity or cytokine assays, which may be performed using samples obtained from a patient before and after treatment.

METHODS FOR DETECTING CANCER

In general, a cancer may be detected in a patient based on the presence of one or
25 more prostate-specific proteins and/or polynucleotides encoding such proteins in a biological sample (for example, blood, sera, urine and/or tumor biopsies) obtained from the patient. In other words, such proteins may be used as markers to indicate the presence or absence of a cancer such as prostate cancer. In addition, such proteins may be useful for the detection of other cancers. The binding agents provided herein generally permit detection of the level of antigen that binds to the
30 agent in the biological sample. Polynucleotide primers and probes may be used to detect the level of mRNA encoding a tumor protein, which is also indicative of the presence or absence of a cancer.

In general, a prostate tumor sequence should be present at a level that is at least three fold higher in tumor tissue than in normal tissue

There are a variety of assay formats known to those of ordinary skill in the art for using a binding agent to detect polypeptide markers in a sample. See, e.g., Harlow and Lane, 5 *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, 1988. In general, the presence or absence of a cancer in a patient may be determined by (a) contacting a biological sample obtained from a patient with a binding agent; (b) detecting in the sample a level of polypeptide that binds to the binding agent; and (c) comparing the level of polypeptide with a predetermined cut-off value.

In a preferred embodiment, the assay involves the use of binding agent immobilized 10 on a solid support to bind to and remove the polypeptide from the remainder of the sample. The bound polypeptide may then be detected using a detection reagent that contains a reporter group and specifically binds to the binding agent/polypeptide complex. Such detection reagents may comprise, for example, a binding agent that specifically binds to the polypeptide or an antibody or other agent that specifically binds to the binding agent, such as an anti-immunoglobulin, protein G, 15 protein A or a lectin. Alternatively, a competitive assay may be utilized, in which a polypeptide is labeled with a reporter group and allowed to bind to the immobilized binding agent after incubation of the binding agent with the sample. The extent to which components of the sample inhibit the binding of the labeled polypeptide to the binding agent is indicative of the reactivity of the sample with the immobilized binding agent. Suitable polypeptides for use within such assays include full 20 length prostate-specific proteins and portions thereof to which the binding agent binds, as described above.

The solid support may be any material known to those of ordinary skill in the art to which the protein may be attached. For example, the solid support may be a test well in a microtiter plate or a nitrocellulose or other suitable membrane. Alternatively, the support may be a bead or 25 disc, such as glass, fiberglass, latex or a plastic material such as polystyrene or polyvinylchloride. The support may also be a magnetic particle or a fiber optic sensor, such as those disclosed, for example, in U.S. Patent No. 5,359,681. The binding agent may be immobilized on the solid support using a variety of techniques known to those of skill in the art, which are amply described in the patent and scientific literature. In the context of the present invention, the term "immobilization" 30 refers to both noncovalent association, such as adsorption, and covalent attachment (which may be a direct linkage between the agent and functional groups on the support or may be a linkage by way of a cross-linking agent). Immobilization by adsorption to a well in a microtiter plate or to a

membrane is preferred. In such cases, adsorption may be achieved by contacting the binding agent, in a suitable buffer, with the solid support for a suitable amount of time. The contact time varies with temperature, but is typically between about 1 hour and about 1 day. In general, contacting a well of a plastic microtiter plate (such as polystyrene or polyvinylchloride) with an amount of binding agent ranging from about 10 ng to about 10 μ g, and preferably about 100 ng to about 1 μ g, is sufficient to immobilize an adequate amount of binding agent.

Covalent attachment of binding agent to a solid support may generally be achieved by first reacting the support with a bifunctional reagent that will react with both the support and a functional group, such as a hydroxyl or amino group, on the binding agent. For example, the binding agent may be covalently attached to supports having an appropriate polymer coating using benzoquinone or by condensation of an aldehyde group on the support with an amine and an active hydrogen on the binding partner (*see, e.g.*, Pierce Immunotechnology Catalog and Handbook, 1991, at A12-A13).

In certain embodiments, the assay is a two-antibody sandwich assay. This assay may be performed by first contacting an antibody that has been immobilized on a solid support, commonly the well of a microtiter plate, with the sample, such that polypeptides within the sample are allowed to bind to the immobilized antibody. Unbound sample is then removed from the immobilized polypeptide-antibody complexes and a detection reagent (preferably a second antibody capable of binding to a different site on the polypeptide) containing a reporter group is added. The amount of detection reagent that remains bound to the solid support is then determined using a method appropriate for the specific reporter group.

More specifically, once the antibody is immobilized on the support as described above, the remaining protein binding sites on the support are typically blocked. Any suitable blocking agent known to those of ordinary skill in the art, such as bovine serum albumin or Tween 20TM (Sigma Chemical Co., St. Louis, MO). The immobilized antibody is then incubated with the sample, and polypeptide is allowed to bind to the antibody. The sample may be diluted with a suitable diluent, such as phosphate-buffered saline (PBS) prior to incubation. In general, an appropriate contact time (*i.e.*, incubation time) is a period of time that is sufficient to detect the presence of polypeptide within a sample obtained from an individual with prostate cancer. Preferably, the contact time is sufficient to achieve a level of binding that is at least about 95% of that achieved at equilibrium between bound and unbound polypeptide. Those of ordinary skill in the art will recognize that the time necessary to achieve equilibrium may be readily determined by

assaying the level of binding that occurs over a period of time. At room temperature, an incubation time of about 30 minutes is generally sufficient.

Unbound sample may then be removed by washing the solid support with an appropriate buffer, such as PBS containing 0.1% Tween 20™. The second antibody, which contains
5 a reporter group, may then be added to the solid support. Preferred reporter groups include those groups recited above.

The detection reagent is then incubated with the immobilized antibody-polypeptide complex for an amount of time sufficient to detect the bound polypeptide. An appropriate amount of time may generally be determined by assaying the level of binding that occurs over a period of
10 time. Unbound detection reagent is then removed and bound detection reagent is detected using the reporter group. The method employed for detecting the reporter group depends upon the nature of the reporter group. For radioactive groups, scintillation counting or autoradiographic methods are generally appropriate. Spectroscopic methods may be used to detect dyes, luminescent groups and fluorescent groups. Biotin may be detected using avidin, coupled to a different reporter group
15 (commonly a radioactive or fluorescent group or an enzyme). Enzyme reporter groups may generally be detected by the addition of substrate (generally for a specific period of time), followed by spectroscopic or other analysis of the reaction products.

To determine the presence or absence of a cancer, such as prostate cancer, the signal detected from the reporter group that remains bound to the solid support is generally compared to a
20 signal that corresponds to a predetermined cut-off value. In one preferred embodiment, the cut-off value for the detection of a cancer is the average mean signal obtained when the immobilized antibody is incubated with samples from patients without the cancer. In general, a sample generating a signal that is three standard deviations above the predetermined cut-off value is considered positive for the cancer. In an alternate preferred embodiment, the cut-off value is
25 determined using a Receiver Operator Curve, according to the method of Sackett et al., *Clinical Epidemiology: A Basic Science for Clinical Medicine*, Little Brown and Co., 1985, p. 106-7. Briefly, in this embodiment, the cut-off value may be determined from a plot of pairs of true positive rates (i.e., sensitivity) and false positive rates (100%-specificity) that correspond to each possible cut-off value for the diagnostic test result. The cut-off value on the plot that is the closest
30 to the upper left-hand corner (i.e., the value that encloses the largest area) is the most accurate cut-off value, and a sample generating a signal that is higher than the cut-off value determined by this method may be considered positive. Alternatively, the cut-off value may be shifted to the left along

the plot, to minimize the false positive rate, or to the right, to minimize the false negative rate. In general, a sample generating a signal that is higher than the cut-off value determined by this method is considered positive for a cancer.

In a related embodiment, the assay is performed in a flow-through or strip test format, wherein the binding agent is immobilized on a membrane, such as nitrocellulose. In the flow-through test, polypeptides within the sample bind to the immobilized binding agent as the sample passes through the membrane. A second, labeled binding agent then binds to the binding agent-polypeptide complex as a solution containing the second binding agent flows through the membrane. The detection of bound second binding agent may then be performed as described above. In the strip test format, one end of the membrane to which binding agent is bound is immersed in a solution containing the sample. The sample migrates along the membrane through a region containing second binding agent and to the area of immobilized binding agent. Concentration of second binding agent at the area of immobilized antibody indicates the presence of a cancer. Typically, the concentration of second binding agent at that site generates a pattern, such as a line, that can be read visually. The absence of such a pattern indicates a negative result. In general, the amount of binding agent immobilized on the membrane is selected to generate a visually discernible pattern when the biological sample contains a level of polypeptide that would be sufficient to generate a positive signal in the two-antibody sandwich assay, in the format discussed above. Preferred binding agents for use in such assays are antibodies and antigen-binding fragments thereof. Preferably, the amount of antibody immobilized on the membrane ranges from about 25 ng to about 1 μ g, and more preferably from about 50 ng to about 500 ng. Such tests can typically be performed with a very small amount of biological sample.

Of course, numerous other assay protocols exist that are suitable for use with the proteins or binding agents of the present invention. The above descriptions are intended to be exemplary only. For example, it will be apparent to those of ordinary skill in the art that the above protocols may be readily modified to use prostate-specific polypeptides to detect antibodies that bind to such polypeptides in a biological sample. The detection of such prostate-specific protein specific antibodies may correlate with the presence of a cancer.

A cancer may also, or alternatively, be detected based on the presence of T cells that specifically react with a prostate-specific protein in a biological sample. Within certain methods, a biological sample comprising CD4⁺ and/or CD8⁺ T cells isolated from a patient is incubated with a prostate-specific polypeptide, a polynucleotide encoding such a polypeptide and/or an APC that

expresses at least an immunogenic portion of such a polypeptide, and the presence or absence of specific activation of the T cells is detected. Suitable biological samples include, but are not limited to, isolated T cells. For example, T cells may be isolated from a patient by routine techniques (such as by Ficoll/Hypaque density gradient centrifugation of peripheral blood lymphocytes). T cells may
5 be incubated *in vitro* for 2-9 days (typically 4 days) at 37°C with prostate-specific polypeptide (e.g., 5 - 25 µg/ml). It may be desirable to incubate another aliquot of a T cell sample in the absence of prostate-specific polypeptide to serve as a control. For CD4⁺ T cells, activation is preferably detected by evaluating proliferation of the T cells. For CD8⁺ T cells, activation is preferably detected by evaluating cytolytic activity. A level of proliferation that is at least two fold greater
10 and/or a level of cytolytic activity that is at least 20% greater than in disease-free patients indicates the presence of a cancer in the patient.

As noted above, a cancer may also, or alternatively, be detected based on the level of mRNA encoding a prostate-specific protein in a biological sample. For example, at least two oligonucleotide primers may be employed in a polymerase chain reaction (PCR) based assay to
15 amplify a portion of a prostate-specific cDNA derived from a biological sample, wherein at least one of the oligonucleotide primers is specific for (*i.e.*, hybridizes to) a polynucleotide encoding the prostate-specific protein. The amplified cDNA is then separated and detected using techniques well known in the art, such as gel electrophoresis. Similarly, oligonucleotide probes that specifically hybridize to a polynucleotide encoding a prostate-specific protein may be used in a hybridization
20 assay to detect the presence of polynucleotide encoding the protein in a biological sample.

To permit hybridization under assay conditions, oligonucleotide primers and probes should comprise an oligonucleotide sequence that has at least about 60%, preferably at least about 75% and more preferably at least about 90%, identity to a portion of a polynucleotide encoding a prostate-specific protein that is at least 10 nucleotides, and preferably at least 20 nucleotides, in
25 length. Preferably, oligonucleotide primers and/or probes will hybridize to a polynucleotide encoding a polypeptide disclosed herein under moderately stringent conditions, as defined above. Oligonucleotide primers and/or probes which may be usefully employed in the diagnostic methods described herein preferably are at least 10-40 nucleotides in length. In a preferred embodiment, the oligonucleotide primers comprise at least 10 contiguous nucleotides, more preferably at least 15
30 contiguous nucleotides, of a DNA molecule having a sequence recited in SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382, 384-476, 524, 526, 530, 531, 533, 535 and 536. Techniques for both PCR based assays and hybridization assays

are well known in the art (*see, for example, Mullis et al., Cold Spring Harbor Symp. Quant. Biol., 51:263, 1987; Erlich ed., PCR Technology, Stockton Press, NY, 1989*).

One preferred assay employs RT-PCR, in which PCR is applied in conjunction with reverse transcription. Typically, RNA is extracted from a biological sample, such as biopsy tissue, and is reverse transcribed to produce cDNA molecules. PCR amplification using at least one specific primer generates a cDNA molecule, which may be separated and visualized using, for example, gel electrophoresis. Amplification may be performed on biological samples taken from a test patient and from an individual who is not afflicted with a cancer. The amplification reaction may be performed on several dilutions of cDNA spanning two orders of magnitude. A two-fold or greater increase in expression in several dilutions of the test patient sample as compared to the same dilutions of the non-cancerous sample is typically considered positive.

In another embodiment, the disclosed compositions may be used as markers for the progression of cancer. In this embodiment, assays as described above for the diagnosis of a cancer may be performed over time, and the change in the level of reactive polypeptide(s) or polynucleotide evaluated. For example, the assays may be performed every 24-72 hours for a period of 6 months to 1 year, and thereafter performed as needed. In general, a cancer is progressing in those patients in whom the level of polypeptide or polynucleotide detected increases over time. In contrast, the cancer is not progressing when the level of reactive polypeptide or polynucleotide either remains constant or decreases with time.

Certain *in vivo* diagnostic assays may be performed directly on a tumor. One such assay involves contacting tumor cells with a binding agent. The bound binding agent may then be detected directly or indirectly via a reporter group. Such binding agents may also be used in histological applications. Alternatively, polynucleotide probes may be used within such applications.

As noted above, to improve sensitivity, multiple prostate-specific protein markers may be assayed within a given sample. It will be apparent that binding agents specific for different proteins provided herein may be combined within a single assay. Further, multiple primers or probes may be used concurrently. The selection of protein markers may be based on routine experiments to determine combinations that results in optimal sensitivity. In addition, or alternatively, assays for proteins provided herein may be combined with assays for other known tumor antigens.

DIAGNOSTIC KITS

The present invention further provides kits for use within any of the above diagnostic methods. Such kits typically comprise two or more components necessary for performing a diagnostic assay. Components may be compounds, reagents, containers and/or equipment. For example, one container within a kit may contain a monoclonal antibody or fragment thereof that specifically binds to a prostate-specific protein. Such antibodies or fragments may be provided attached to a support material, as described above. One or more additional containers may enclose elements, such as reagents or buffers, to be used in the assay. Such kits may also, or alternatively, contain a detection reagent as described above that contains a reporter group suitable for direct or indirect detection of antibody binding.

Alternatively, a kit may be designed to detect the level of mRNA encoding a prostate-specific protein in a biological sample. Such kits generally comprise at least one oligonucleotide probe or primer, as described above, that hybridizes to a polynucleotide encoding a prostate-specific protein. Such an oligonucleotide may be used, for example, within a PCR or hybridization assay. Additional components that may be present within such kits include a second oligonucleotide and/or a diagnostic reagent or container to facilitate the detection of a polynucleotide encoding a prostate-specific protein.

The following Examples are offered by way of illustration and not by way of limitation.

EXAMPLES

EXAMPLE 1

5 ISOLATION AND CHARACTERIZATION OF PROSTATE-SPECIFIC POLYPEPTIDES

This Example describes the isolation of certain prostate-specific polypeptides from a prostate tumor cDNA library.

A human prostate tumor cDNA expression library was constructed from prostate
10 tumor poly A⁺ RNA using a Superscript Plasmid System for cDNA Synthesis and Plasmid Cloning kit (BRL Life Technologies, Gaithersburg, MD 20897) following the manufacturer's protocol. Specifically, prostate tumor tissues were homogenized with polytron (Kinematica, Switzerland) and total RNA was extracted using Trizol reagent (BRL Life Technologies) as directed by the manufacturer. The poly A⁺ RNA was then purified using a Qiagen oligotex spin column mRNA
15 purification kit (Qiagen, Santa Clarita, CA 91355) according to the manufacturer's protocol. First-strand cDNA was synthesized using the NotI/Oligo-dT18 primer. Double-stranded cDNA was synthesized, ligated with EcoRI/BAXI adaptors (Invitrogen, San Diego, CA) and digested with NotI. Following size fractionation with Chroma Spin-1000 columns (Clontech, Palo Alto, CA), the cDNA was ligated into the EcoRI/NotI site of pCDNA3.1 (Invitrogen) and transformed into
20 ElectroMax *E. coli* DH10B cells (BRL Life Technologies) by electroporation.

Using the same procedure, a normal human pancreas cDNA expression library was prepared from a pool of six tissue specimens (Clontech). The cDNA libraries were characterized by determining the number of independent colonies, the percentage of clones that carried insert, the average insert size and by sequence analysis. The prostate tumor library contained 1.64×10^7
25 independent colonies, with 70% of clones having an insert and the average insert size being 1745 base pairs. The normal pancreas cDNA library contained 3.3×10^6 independent colonies, with 69% of clones having inserts and the average insert size being 1120 base pairs. For both libraries, sequence analysis showed that the majority of clones had a full length cDNA sequence and were synthesized from mRNA, with minimal rRNA and mitochondrial DNA contamination.

30 cDNA library subtraction was performed using the above prostate tumor and normal pancreas cDNA libraries, as described by Hara *et al.* (*Blood*, 84:189-199, 1994) with some modifications. Specifically, a prostate tumor-specific subtracted cDNA library was generated as

follows. Normal pancreas cDNA library (70 µg) was digested with EcoRI, NotI, and SfuI, followed by a filling-in reaction with DNA polymerase Klenow fragment. After phenol-chloroform extraction and ethanol precipitation, the DNA was dissolved in 100 µl of H₂O, heat-denatured and mixed with 100 µl (100 µg) of Photoprobe biotin (Vector Laboratories, Burlingame, CA). As
5 recommended by the manufacturer, the resulting mixture was irradiated with a 270 W sunlamp on ice for 20 minutes. Additional Photoprobe biotin (50 µl) was added and the biotinylation reaction was repeated. After extraction with butanol five times, the DNA was ethanol-precipitated and dissolved in 23 µl H₂O to form the driver DNA.

To form the tracer DNA, 10 µg prostate tumor cDNA library was digested with
10 BamHI and XhoI, phenol chloroform extracted and passed through Chroma spin-400 columns (Clontech). Following ethanol precipitation, the tracer DNA was dissolved in 5 µl H₂O. Tracer DNA was mixed with 15 µl driver DNA and 20 µl of 2 x hybridization buffer (1.5 M NaCl/10 mM EDTA/50 mM HEPES pH 7.5/0.2% sodium dodecyl sulfate), overlaid with mineral oil, and heat-denatured completely. The sample was immediately transferred into a 68 °C water bath and
15 incubated for 20 hours (long hybridization [LH]). The reaction mixture was then subjected to a streptavidin treatment followed by phenol/chloroform extraction. This process was repeated three more times. Subtracted DNA was precipitated, dissolved in 12 µl H₂O, mixed with 8 µl driver DNA and 20 µl of 2 x hybridization buffer, and subjected to a hybridization at 68 °C for 2 hours (short hybridization [SH]). After removal of biotinylated double-stranded DNA, subtracted cDNA
20 was ligated into BamHI/XhoI site of chloramphenicol resistant pBCSK⁺ (Stratagene, La Jolla, CA 92037) and transformed into ElectroMax *E. coli* DH10B cells by electroporation to generate a prostate tumor specific subtracted cDNA library (referred to as "prostate subtraction I").

To analyze the subtracted cDNA library, plasmid DNA was prepared from 100 independent clones, randomly picked from the subtracted prostate tumor specific library and
25 grouped based on insert size. Representative cDNA clones were further characterized by DNA sequencing with a Perkin Elmer/Applied Biosystems Division Automated Sequencer Model 373A (Foster City, CA). Six cDNA clones, hereinafter referred to as F1-13, F1-12, F1-16, H1-1, H1-9 and H1-4, were shown to be abundant in the subtracted prostate-specific cDNA library. The determined 3' and 5' cDNA sequences for F1-12 are provided in SEQ ID NO: 2 and 3, respectively,
30 with determined 3' cDNA sequences for F1-13, F1-16, H1-1, H1-9 and H1-4 being provided in SEQ ID NO: 1 and 4-7, respectively.

The cDNA sequences for the isolated clones were compared to known sequences in the gene bank using the EMBL and GenBank databases (release 96). Four of the prostate tumor cDNA clones, F1-13, F1-16, H1-1, and H1-4, were determined to encode the following previously identified proteins: prostate specific antigen (PSA), human glandular kallikrein, human tumor expression enhanced gene, and mitochondria cytochrome C oxidase subunit II. H1-9 was found to be identical to a previously identified human autonomously replicating sequence. No significant homologies to the cDNA sequence for F1-12 were found.

Subsequent studies led to the isolation of a full-length cDNA sequence for F1-12. This sequence is provided in SEQ ID NO: 107, with the corresponding predicted amino acid sequence being provided in SEQ ID NO: 108.

To clone less abundant prostate tumor specific genes, cDNA library subtraction was performed by subtracting the prostate tumor cDNA library described above with the normal pancreas cDNA library and with the three most abundant genes in the previously subtracted prostate tumor specific cDNA library: human glandular kallikrein, prostate specific antigen (PSA), and mitochondria cytochrome C oxidase subunit II. Specifically, 1 μ g each of human glandular kallikrein, PSA and mitochondria cytochrome C oxidase subunit II cDNAs in pCDNA3.1 were added to the driver DNA and subtraction was performed as described above to provide a second subtracted cDNA library hereinafter referred to as the "subtracted prostate tumor specific cDNA library with spike".

Twenty-two cDNA clones were isolated from the subtracted prostate tumor specific cDNA library with spike. The determined 3' and 5' cDNA sequences for the clones referred to as J1-17, L1-12, N1-1862, J1-13, J1-19, J1-25, J1-24, K1-58, K1-63, L1-4 and L1-14 are provided in SEQ ID NOS: 8-9, 10-11, 12-13, 14-15, 16-17, 18-19, 20-21, 22-23, 24-25, 26-27 and 28-29, respectively. The determined 3' cDNA sequences for the clones referred to as J1-12, J1-16, J1-21, K1-48, K1-55, L1-2, L1-6, N1-1858, N1-1860, N1-1861, N1-1864 are provided in SEQ ID NOS: 30-40, respectively. Comparison of these sequences with those in the gene bank as described above, revealed no significant homologies to three of the five most abundant DNA species, (J1-17, L1-12 and N1-1862; SEQ ID NOS: 8-9, 10-11 and 12-13, respectively). Of the remaining two most abundant species, one (J1-12; SEQ ID NO:30) was found to be identical to the previously identified human pulmonary surfactant-associated protein, and the other (K1-48; SEQ ID NO:33) was determined to have some homology to *R. norvegicus* mRNA for 2-arylpropionyl-CoA epimerase. Of the 17 less abundant cDNA clones isolated from the subtracted prostate tumor specific cDNA

library with spike, four (J1-16, K1-55, L1-6 and N1-1864; SEQ ID NOS:31, 34, 36 and 40, respectively) were found to be identical to previously identified sequences, two (J1-21 and N1-1860; SEQ ID NOS: 32 and 38, respectively) were found to show some homology to non-human sequences, and two (L1-2 and N1-1861; SEQ ID NOS: 35 and 39, respectively) were found to show
5 some homology to known human sequences. No significant homologies were found to the polypeptides J1-13, J1-19, J1-24, J1-25, K1-58, K1-63, L1-4, L1-14 (SEQ ID NOS: 14-15, 16-17, 20-21, 18-19, 22-23, 24-25, 26-27, 28-29, respectively).

Subsequent studies led to the isolation of full length cDNA sequences for J1-17, L1-12 and N1-1862 (SEQ ID NOS: 109-111, respectively). The corresponding predicted amino acid
10 sequences are provided in SEQ ID NOS: 112-114. L1-12 is also referred to as P501S.

In a further experiment, four additional clones were identified by subtracting a prostate tumor cDNA library with normal prostate cDNA prepared from a pool of three normal prostate poly A+ RNA (referred to as "prostate subtraction 2"). The determined cDNA sequences for these clones, hereinafter referred to as U1-3064, U1-3065, V1-3692 and 1A-3905, are provided
15 in SEQ ID NO: 69-72, respectively. Comparison of the determined sequences with those in the gene bank revealed no significant homologies to U1-3065.

A second subtraction with spike (referred to as "prostate subtraction spike 2") was performed by subtracting a prostate tumor specific cDNA library with spike with normal pancreas cDNA library and further spiked with PSA, J1-17, pulmonary surfactant-associated protein, mitochondrial DNA, cytochrome c oxidase subunit II, N1-1862, autonomously replicating
20 sequence, L1-12 and tumor expression enhanced gene. Four additional clones, hereinafter referred to as V1-3686, R1-2330, 1B-3976 and V1-3679, were isolated. The determined cDNA sequences for these clones are provided in SEQ ID NO:73-76, respectively. Comparison of these sequences with those in the gene bank revealed no significant homologies to V1-3686 and R1-2330.

Further analysis of the three prostate subtractions described above (prostate subtraction 2, subtracted prostate tumor specific cDNA library with spike, and prostate subtraction spike 2) resulted in the identification of sixteen additional clones, referred to as 1G-4736, 1G-4738, 1G-4741, 1G-4744, 1G-4734, 1H-4774, 1H-4781, 1H-4785, 1H-4787, 1H-4796, 1I-4810, 1I-4811, 1J-4876, 1K-4884 and 1K-4896. The determined cDNA sequences for these clones are provided in
25 SEQ ID NOS: 77-92, respectively. Comparison of these sequences with those in the gene bank as described above, revealed no significant homologies to 1G-4741, 1G-4734, 1I-4807, 1J-4876 and 1K-4896 (SEQ ID NOS: 79, 81, 87, 90 and 92, respectively). Further analysis of the isolated
30

clones led to the determination of extended cDNA sequences for 1G-4736, 1G-4738, 1G-4741, 1G-4744, 1H-4774, 1H-4781, 1H-4785, 1H-4787, 1H-4796, 1I-4807, 1J-4876, 1K-4884 and 1K-4896, provided in SEQ ID NOS: 179-188 and 191-193, respectively, and to the determination of additional partial cDNA sequences for 1I-4810 and 1I-4811, provided in SEQ ID NOS: 189 and
5 190, respectively.

Additional studies with prostate subtraction spike 2 resulted in the isolation of three more clones. Their sequences were determined as described above and compared to the most recent GenBank. All three clones were found to have homology to known genes, which are Cysteine-rich protein, KIAA0242, and KIAA0280 (SEQ ID NO: 317, 319, and 320, respectively). Further
10 analysis of these clones by Synteni microarray (Synteni, Palo Alto, CA) demonstrated that all three clones were over-expressed in most prostate tumors and prostate BPH, as well as in the majority of normal prostate tissues tested, but low expression in all other normal tissues.

An additional subtraction was performed by subtracting a normal prostate cDNA library with normal pancreas cDNA (referred to as "prostate subtraction 3"). This led to the
15 identification of six additional clones referred to as 1G-4761, 1G-4762, 1H-4766, 1H-4770, 1H-4771 and 1H-4772 (SEQ ID NOS: 93-98). Comparison of these sequences with those in the gene bank revealed no significant homologies to 1G-4761 and 1H-4771 (SEQ ID NOS: 93 and 97, respectively). Further analysis of the isolated clones led to the determination of extended cDNA sequences for 1G-4761, 1G-4762, 1H-4766 and 1H-4772 provided in SEQ ID NOS: 194-196 and
20 199, respectively, and to the determination of additional partial cDNA sequences for 1H-4770 and 1H-4771, provided in SEQ ID NOS: 197 and 198, respectively.

Subtraction of a prostate tumor cDNA library, prepared from a pool of polyA+ RNA from three prostate cancer patients, with a normal pancreas cDNA library (prostate subtraction 4) led to the identification of eight clones, referred to as 1D-4297, 1D-4309, 1D-4278, 1D-4288, 1D-
25 4283, 1D-4304, 1D-4296 and 1D-4280 (SEQ ID NOS: 99-107). These sequences were compared to those in the gene bank as described above. No significant homologies were found to 1D-4283 and 1D-4304 (SEQ ID NOS: 103 and 104, respectively). Further analysis of the isolated clones led to the determination of extended cDNA sequences for 1D-4309, 1D-4278, 1D-4288, 1D-4283, 1D-4304, 1D-4296 and 1D-4280, provided in SEQ ID NOS: 200-206, respectively.

30 cDNA clones isolated in prostate subtraction 1 and prostate subtraction 2, described above, were colony PCR amplified and their mRNA expression levels in prostate tumor, normal prostate and in various other normal tissues were determined using microarray technology (Synteni,

Palo Alto, CA). Briefly, the PCR amplification products were dotted onto slides in an array format, with each product occupying a unique location in the array. mRNA was extracted from the tissue sample to be tested, reverse transcribed, and fluorescent-labeled cDNA probes were generated. The microarrays were probed with the labeled cDNA probes, the slides scanned and fluorescence intensity was measured. This intensity correlates with the hybridization intensity. Two clones (referred to as P509S and P510S) were found to be over-expressed in prostate tumor and normal prostate and expressed at low levels in all other normal tissues tested (liver, pancreas, skin, bone marrow, brain, breast, adrenal gland, bladder, testes, salivary gland, large intestine, kidney, ovary, lung, spinal cord, skeletal muscle and colon). The determined cDNA sequences for P509S and P510S are provided in SEQ ID NO: 223 and 224, respectively. Comparison of these sequences with those in the gene bank as described above, revealed some homology to previously identified ESTs.

Additional, studies led to the isolation of the full-length cDNA sequence for P509S. This sequence is provided in SEQ ID NO: 332, with the corresponding predicted amino acid sequence being provided in SEQ ID NO: 339. Two variant full-length cDNA sequences for P510S are provided in SEQ ID NO: 535 and 536, with the corresponding predicted amino acid sequences being provided in SEQ ID NO: 537 and 538, respectively.

EXAMPLE 2

DETERMINATION OF TISSUE SPECIFICITY OF PROSTATE-SPECIFIC POLYPEPTIDES

Using gene specific primers, mRNA expression levels for the representative prostate-specific polypeptides F1-16, H1-1, J1-17 (also referred to as P502S), L1-12 (also referred to as P501S), F1-12 (also referred to as P504S) and N1-1862 (also referred to as P503S) were examined in a variety of normal and tumor tissues using RT-PCR.

Briefly, total RNA was extracted from a variety of normal and tumor tissues using Trizol reagent as described above. First strand synthesis was carried out using 1-2 μ g of total RNA with SuperScript II reverse transcriptase (BRL Life Technologies) at 42 °C for one hour. The cDNA was then amplified by PCR with gene-specific primers. To ensure the semi-quantitative nature of the RT-PCR, β -actin was used as an internal control for each of the tissues examined. First, serial dilutions of the first strand cDNAs were prepared and RT-PCR assays were performed using β -actin specific primers. A dilution was then chosen that enabled the linear range amplification of the β -actin template and which was sensitive enough to reflect the differences in the initial copy numbers. Using these conditions, the β -actin levels were determined for each

reverse transcription reaction from each tissue. DNA contamination was minimized by DNase treatment and by assuring a negative PCR result when using first strand cDNA that was prepared without adding reverse transcriptase.

mRNA Expression levels were examined in four different types of tumor tissue (prostate tumor from 2 patients, breast tumor from 3 patients, colon tumor, lung tumor), and sixteen different normal tissues, including prostate, colon, kidney, liver, lung, ovary, pancreas, skeletal muscle, skin, stomach, testes, bone marrow and brain. F1-16 was found to be expressed at high levels in prostate tumor tissue, colon tumor and normal prostate, and at lower levels in normal liver, skin and testes, with expression being undetectable in the other tissues examined. H1-1 was found to be expressed at high levels in prostate tumor, lung tumor, breast tumor, normal prostate, normal colon and normal brain, at much lower levels in normal lung, pancreas, skeletal muscle, skin, small intestine, bone marrow, and was not detected in the other tissues tested. J1-17 (P502S) and L1-12 (P501S) appear to be specifically over-expressed in prostate, with both genes being expressed at high levels in prostate tumor and normal prostate but at low to undetectable levels in all the other tissues examined. N1-1862 (P503S) was found to be over-expressed in 60% of prostate tumors and detectable in normal colon and kidney. The RT-PCR results thus indicate that F1-16, H1-1, J1-17 (P502S), N1-1862 (P503S) and L1-12 (P501S) are either prostate specific or are expressed at significantly elevated levels in prostate.

Further RT-PCR studies showed that F1-12 (P504S) is over-expressed in 60% of prostate tumors, detectable in normal kidney but not detectable in all other tissues tested. Similarly, R1-2330 was shown to be over-expressed in 40% of prostate tumors, detectable in normal kidney and liver, but not detectable in all other tissues tested. U1-3064 was found to be over-expressed in 60% of prostate tumors, and also expressed in breast and colon tumors, but was not detectable in normal tissues.

RT-PCR characterization of R1-2330, U1-3064 and 1D-4279 showed that these three antigens are over-expressed in prostate and/or prostate tumors.

Northern analysis with four prostate tumors, two normal prostate samples, two BPH prostates, and normal colon, kidney, liver, lung, pancreas, skeletal muscle, brain, stomach, testes, small intestine and bone marrow, showed that L1-12 (P501S) is over-expressed in prostate tumors and normal prostate, while being undetectable in other normal tissues tested. J1-17 (P502S) was detected in two prostate tumors and not in the other tissues tested. N1-1862 (P503S) was found to be over-expressed in three prostate tumors and to be expressed in normal prostate, colon and kidney,

but not in other tissues tested. F1-12 (P504S) was found to be highly expressed in two prostate tumors and to be undetectable in all other tissues tested.

The microarray technology described above was used to determine the expression levels of representative antigens described herein in prostate tumor, breast tumor and the following normal tissues: prostate, liver, pancreas, skin, bone marrow, brain, breast, adrenal gland, bladder, testes, salivary gland, large intestine, kidney, ovary, lung, spinal cord, skeletal muscle and colon. L1-12 (P501S) was found to be over-expressed in normal prostate and prostate tumor, with some expression being detected in normal skeletal muscle. Both J1-12 and F1-12 (P504S) were found to be over-expressed in prostate tumor, with expression being lower or undetectable in all other tissues tested. N1-1862 (P503S) was found to be expressed at high levels in prostate tumor and normal prostate, and at low levels in normal large intestine and normal colon, with expression being undetectable in all other tissues tested. R1-2330 was found to be over-expressed in prostate tumor and normal prostate, and to be expressed at lower levels in all other tissues tested. 1D-4279 was found to be over-expressed in prostate tumor and normal prostate, expressed at lower levels in normal spinal cord, and to be undetectable in all other tissues tested.

Further microarray analysis to specifically address the extent to which P501S (SEQ ID NO: 110) was expressed in breast tumor revealed moderate over-expression not only in breast tumor, but also in metastatic breast tumor (2/31), with negligible to low expression in normal tissues. This data suggests that P501S may be over-expressed in various breast tumors as well as in prostate tumors.

The expression levels of 32 ESTs (expressed sequence tags) described by Vasmatzis *et al.* (*Proc. Natl. Acad. Sci. USA* 95:300-304, 1998) in a variety of tumor and normal tissues were examined by microarray technology as described above. Two of these clones (referred to as P1000C and P1001C) were found to be over-expressed in prostate tumor and normal prostate, and expressed at low to undetectable levels in all other tissues tested (normal aorta, thymus, resting and activated PBMC, epithelial cells, spinal cord, adrenal gland, fetal tissues, skin, salivary gland, large intestine, bone marrow, liver, lung, dendritic cells, stomach, lymph nodes, brain, heart, small intestine, skeletal muscle, colon and kidney. The determined cDNA sequences for P1000C and P1001C are provided in SEQ ID NO: 384 and 472, respectively. The sequence of P1001C was found to show some homology to the previously isolated Human mRNA for JM27 protein. No significant homologies were found to the sequence of P1000C.

The expression of the polypeptide encoded by the full length cDNA sequence for F1-12 (also referred to as P504S; SEQ ID NO: 108) was investigated by immunohistochemical analysis. Rabbit-anti-P504S polyclonal antibodies were generated against the full length P504S protein by standard techniques. Subsequent isolation and characterization of the polyclonal antibodies were also performed by techniques well known in the art. Immunohistochemical analysis showed that the P504S polypeptide was expressed in 100% of prostate carcinoma samples tested (n=5).

The rabbit-anti-P504S polyclonal antibody did not appear to label benign prostate cells with the same cytoplasmic granular staining, but rather with light nuclear staining. Analysis of normal tissues revealed that the encoded polypeptide was found to be expressed in some, but not all normal human tissues. Positive cytoplasmic staining with rabbit-anti-P504S polyclonal antibody was found in normal human kidney, liver, brain, colon and lung-associated macrophages, whereas heart and bone marrow were negative.

This data indicates that the P504S polypeptide is present in prostate cancer tissues, and that there are qualitative and quantitative differences in the staining between benign prostatic hyperplasia tissues and prostate cancer tissues, suggesting that this polypeptide may be detected selectively in prostate tumors and therefore be useful in the diagnosis of prostate cancer.

EXAMPLE 3

ISOLATION AND CHARACTERIZATION OF PROSTATE-SPECIFIC POLYPEPTIDES BY PCR-BASED SUBTRACTION

A cDNA subtraction library, containing cDNA from normal prostate subtracted with ten other normal tissue cDNAs (brain, heart, kidney, liver, lung, ovary, placenta, skeletal muscle, spleen and thymus) and then submitted to a first round of PCR amplification, was purchased from Clontech. This library was subjected to a second round of PCR amplification, following the manufacturer's protocol. The resulting cDNA fragments were subcloned into the vector pT7 Blue T-vector (Novagen, Madison, WI) and transformed into XL-1 Blue MRF' *E. coli* (Stratagene). DNA was isolated from independent clones and sequenced using a Perkin Elmer/Applied Biosystems Division Automated Sequencer Model 373A.

Fifty-nine positive clones were sequenced. Comparison of the DNA sequences of these clones with those in the gene bank, as described above, revealed no significant homologies to 25 of these clones, hereinafter referred to as P5, P8, P9, P18, P20, P30, P34, P36, P38, P39, P42, P49, P50, P53, P55, P60, P64, P65, P73, P75, P76, P79 and P84. The determined cDNA sequences
5 for these clones are provided in SEQ ID NO: 41-45, 47-52 and 54-65, respectively. P29, P47, P68, P80 and P82 (SEQ ID NO: 46, 53 and 66-68, respectively) were found to show some degree of homology to previously identified DNA sequences. To the best of the inventors' knowledge, none of these sequences have been previously shown to be present in prostate.

Further studies using the PCR-based methodology described above resulted in the
10 isolation of more than 180 additional clones, of which 23 clones were found to show no significant homologies to known sequences. The determined cDNA sequences for these clones are provided in SEQ ID NO: 115-123, 127, 131, 137, 145, 147-151, 153, 156-158 and 160. Twenty-three clones (SEQ ID NO: 124-126, 128-130, 132-136, 138-144, 146, 152, 154, 155 and 159) were found to show some homology to previously identified ESTs. An additional ten clones (SEQ ID NO: 161-
15 170) were found to have some degree of homology to known genes. Larger cDNA clones containing the P20 sequence represent splice variants of a gene referred to as P703P. The determined DNA sequence for the variants referred to as DE1, DE13 and DE14 are provided in SEQ ID NOS: 171, 175 and 177, respectively, with the corresponding predicted amino acid sequences being provided in SEQ ID NO: 172, 176 and 178, respectively. The determined cDNA
20 sequence for an extended spliced form of P703 is provided in SEQ ID NO: 225. The DNA sequences for the splice variants referred to as DE2 and DE6 are provided in SEQ ID NOS: 173 and 174, respectively.

mRNA Expression levels for representative clones in tumor tissues (prostate (n=5), breast (n=2), colon and lung) normal tissues (prostate (n=5), colon, kidney, liver, lung (n=2), ovary
25 (n=2), skeletal muscle, skin, stomach, small intestine and brain), and activated and non-activated PBMC was determined by RT-PCR as described above. Expression was examined in one sample of each tissue type unless otherwise indicated.

P9 was found to be highly expressed in normal prostate and prostate tumor compared to all normal tissues tested except for normal colon which showed comparable expression. P20, a
30 portion of the P703P gene, was found to be highly expressed in normal prostate and prostate tumor, compared to all twelve normal tissues tested. A modest increase in expression of P20 in breast tumor (n=2), colon tumor and lung tumor was seen compared to all normal tissues except lung (1 of

2). Increased expression of P18 was found in normal prostate, prostate tumor and breast tumor compared to other normal tissues except lung and stomach. A modest increase in expression of P5 was observed in normal prostate compared to most other normal tissues. However, some elevated expression was seen in normal lung and PBMC. Elevated expression of P5 was also observed in prostate tumors (2 of 5), breast tumor and one lung tumor sample. For P30, similar expression levels were seen in normal prostate and prostate tumor, compared to six of twelve other normal tissues tested. Increased expression was seen in breast tumors, one lung tumor sample and one colon tumor sample, and also in normal PBMC. P29 was found to be over-expressed in prostate tumor (5 of 5) and normal prostate (5 of 5) compared to the majority of normal tissues. However, substantial expression of P29 was observed in normal colon and normal lung (2 of 2). P80 was found to be over-expressed in prostate tumor (5 of 5) and normal prostate (5 of 5) compared to all other normal tissues tested, with increased expression also being seen in colon tumor.

Further studies resulted in the isolation of twelve additional clones, hereinafter referred to as 10-d8, 10-h10, 11-c8, 7-g6, 8-b5, 8-b6, 8-d4, 8-d9, 8-g3, 8-h11, 9-f12 and 9-f3. The determined DNA sequences for 10-d8, 10-h10, 11-c8, 8-d4, 8-d9, 8-h11, 9-f12 and 9-f3 are provided in SEQ ID NO: 207, 208, 209, 216, 217, 220, 221 and 222, respectively. The determined forward and reverse DNA sequences for 7-g6, 8-b5, 8-b6 and 8-g3 are provided in SEQ ID NO: 210 and 211; 212 and 213; 214 and 215; and 218 and 219, respectively. Comparison of these sequences with those in the gene bank revealed no significant homologies to the sequence of 9-f3. The clones 10-d8, 11-c8 and 8-h11 were found to show some homology to previously isolated ESTs, while 10-h10, 8-b5, 8-b6, 8-d4, 8-d9, 8-g3 and 9-f12 were found to show some homology to previously identified genes. Further characterization of 7-G6 and 8-G3 showed identity to the known genes PAP and PSA, respectively.

mRNA expression levels for these clones were determined using the micro-array technology described above. The clones 7-G6, 8-G3, 8-B5, 8-B6, 8-D4, 8-D9, 9-F3, 9-F12, 9-H3, 10-A2, 10-A4, 11-C9 and 11-F2 were found to be over-expressed in prostate tumor and normal prostate, with expression in other tissues tested being low or undetectable. Increased expression of 8-F11 was seen in prostate tumor and normal prostate, bladder, skeletal muscle and colon. Increased expression of 10-H10 was seen in prostate tumor and normal prostate, bladder, lung, colon, brain and large intestine. Increased expression of 9-B1 was seen in prostate tumor, breast tumor, and normal prostate, salivary gland, large intestine and skin, with increased expression of 11-C8 being seen in prostate tumor, and normal prostate and large intestine.

An additional cDNA fragment derived from the PCR-based normal prostate subtraction, described above, was found to be prostate specific by both micro-array technology and RT-PCR. The determined cDNA sequence of this clone (referred to as 9-A11) is provided in SEQ ID NO: 226. Comparison of this sequence with those in the public databases revealed 99% identity to the known gene HOXB13.

Further studies led to the isolation of the clones 8-C6 and 8-H7. The determined cDNA sequences for these clones are provided in SEQ ID NO: 227 and 228, respectively. These sequences were found to show some homology to previously isolated ESTs.

PCR and hybridization-based methodologies were employed to obtain longer cDNA sequences for clone P20 (also referred to as P703P), yielding three additional cDNA fragments that progressively extend the 5' end of the gene. These fragments, referred to as P703PDE5, P703P6.26, and P703PX-23 (SEQ ID NO: 326, 328 and 330, with the predicted corresponding amino acid sequences being provided in SEQ ID NO: 327, 329 and 331, respectively) contain additional 5' sequence. P703PDE5 was recovered by screening of a cDNA library (#141-26) with a portion of P703P as a probe. P703P6.26 was recovered from a mixture of three prostate tumor cDNAs and P703PX_23 was recovered from cDNA library (#438-48). Together, the additional sequences include all of the putative mature serine protease along with part of the putative signal sequence. The putative full-length cDNA sequence for P703P is provided in SEQ ID NO: 524, with the corresponding predicted amino acid sequence being provided in SEQ ID NO: 525.

Further studies using a PCR-based subtraction library of a prostate tumor pool subtracted against a pool of normal tissues (referred to as JP: PCR subtraction) resulted in the isolation of thirteen additional clones, seven of which did not share any significant homology to known GenBank sequences. The determined cDNA sequences for these seven clones (P711P, P712P, novel 23, P774P, P775P, P710P and P768P) are provided in SEQ ID NO: 307-311, 313 and 315, respectively. The remaining six clones (SEQ ID NO: 316 and 321-325) were shown to share some homology to known genes. By microarray analysis, all thirteen clones showed three or more fold over-expression in prostate tissues, including prostate tumors, BPH and normal prostate as compared to normal non-prostate tissues. Clones P711P, P712P, novel 23 and P768P showed over-expression in most prostate tumors and BPH tissues tested (n=29), and in the majority of normal prostate tissues (n=4), but background to low expression levels in all normal tissues. Clones P774P, P775P and P710P showed comparatively lower expression and expression in fewer prostate tumors and BPH samples, with negative to low expression in normal prostate.

The full-length cDNA for P711P was obtained by employing the partial sequence of SEQ ID NO: 307 to screen a prostate cDNA library. Specifically, a directionally cloned prostate cDNA library was prepared using standard techniques. One million colonies of this library were plated onto LB/Amp plates. Nylon membrane filters were used to lift these colonies, and the cDNAs which were picked up by these filters were denatured and cross-linked to the filters by UV light. The P711P cDNA fragment of SEQ ID NO: 307 was radio-labeled and used to hybridize with these filters. Positive clones were selected, and cDNAs were prepared and sequenced using an automatic Perkin Elmer/Applied Biosystems sequencer. The determined full-length sequence of P711P is provided in SEQ ID NO: 382, with the corresponding predicted amino acid sequence being provided in SEQ ID NO: 383.

Using PCR and hybridization-based methodologies, additional cDNA sequence information was derived for two clones described above, 11-C9 and 9-F3, herein after referred to as P707P and P714P, respectively (SEQ ID NO: 333 and 334). After comparison with the most recent GenBank, P707P was found to be a splice variant of the known gene HoxB13. In contrast, no significant homologies to P714P were found.

Clones 8-B3, P89, P98, P130 and P201 (as disclosed in U.S. Patent Application No. 09/020,956, filed February 9, 1998) were found to be contained within one contiguous sequence, referred to as P705P (SEQ ID NO: 335, with the predicted amino acid sequence provided in SEQ ID NO: 336), which was determined to be a splice variant of the known gene NKX 3.1.

Further studies on P775P resulted in the isolation of four additional sequences (SEQ ID NO: 473-476) which are all splice variants of the P775P gene. The sequence of SEQ ID NO: 474 was found to contain two open reading frames (ORFs). The predicted amino acid sequences encoded by these ORFs are provided in SEQ ID NO: 477 and 478. The cDNA sequence of SEQ ID NO: 475 was found to contain an ORF which encodes the amino acid sequence of SEQ ID NO: 479. The cDNA sequence of SEQ ID NO: 473 was found to contain four ORFs. The predicted amino acid sequences encoded by these ORFs are provided in SEQ ID NO: 480-483.

Subsequent studies led to the identification of a genomic region on chromosome 22q11.2, known as the Cat Eye Syndrome region, that contains the five prostate genes P704P, P712P, P774P, P775P and B305D. The relative location of each of these five genes within the genomic region is shown in Fig. 10. This region may therefore be associated with malignant tumors, and other potential tumor genes may be contained within this region. These studies also led

to the identification of a potential open reading frame (ORF) for P775P (provided in SEQ ID NO: 533), which encodes the amino acid sequence of SEQ ID NO: 534.

EXAMPLE 4

SYNTHESIS OF POLYPEPTIDES

Polypeptides may be synthesized on a Perkin Elmer/Applied Biosystems 430A peptide synthesizer using Fmoc chemistry with HPTU (O-Benzotriazole-N,N,N',N'-tetramethyluronium hexafluorophosphate) activation. A Gly-Cys-Gly sequence may be attached to the amino terminus of the peptide to provide a method of conjugation, binding to an immobilized surface, or labeling of the peptide. Cleavage of the peptides from the solid support may be carried out using the following cleavage mixture: trifluoroacetic acid:ethanedithiol:thioanisole:water:phenol (40:1:2:2:3). After cleaving for 2 hours, the peptides may be precipitated in cold methyl-t-butyl-ether. The peptide pellets may then be dissolved in water containing 0.1% trifluoroacetic acid (TFA) and lyophilized prior to purification by C18 reverse phase HPLC. A gradient of 0%-60% acetonitrile (containing 0.1% TFA) in water (containing 0.1% TFA) may be used to elute the peptides. Following lyophilization of the pure fractions, the peptides may be characterized using electrospray or other types of mass spectrometry and by amino acid analysis.

EXAMPLE 5

FURTHER ISOLATION AND CHARACTERIZATION OF PROSTATE-SPECIFIC POLYPEPTIDES BY PCR-BASED SUBTRACTION

A cDNA library generated from prostate primary tumor mRNA as described above was subtracted with cDNA from normal prostate. The subtraction was performed using a PCR-based protocol (Clontech), which was modified to generate larger fragments. Within this protocol, tester and driver double stranded cDNA were separately digested with five restriction enzymes that recognize six-nucleotide restriction sites (MluI, MscI, PvuII, SalI and StuI). This digestion resulted in an average cDNA size of 600 bp, rather than the average size of 300 bp that results from digestion with RsaI according to the Clontech protocol. This modification did not affect the

subtraction efficiency. Two tester populations were then created with different adapters, and the driver library remained without adapters.

The tester and driver libraries were then hybridized using excess driver cDNA. In the first hybridization step, driver was separately hybridized with each of the two tester cDNA populations. This resulted in populations of (a) unhybridized tester cDNAs, (b) tester cDNAs hybridized to other tester cDNAs, (c) tester cDNAs hybridized to driver cDNAs and (d) unhybridized driver cDNAs. The two separate hybridization reactions were then combined, and rehybridized in the presence of additional denatured driver cDNA. Following this second hybridization, in addition to populations (a) through (d), a fifth population (e) was generated in which tester cDNA with one adapter hybridized to tester cDNA with the second adapter. Accordingly, the second hybridization step resulted in enrichment of differentially expressed sequences which could be used as templates for PCR amplification with adaptor-specific primers.

The ends were then filled in, and PCR amplification was performed using adaptor-specific primers. Only population (e), which contained tester cDNA that did not hybridize to driver cDNA, was amplified exponentially. A second PCR amplification step was then performed, to reduce background and further enrich differentially expressed sequences.

This PCR-based subtraction technique normalizes differentially expressed cDNAs so that rare transcripts that are overexpressed in prostate tumor tissue may be recoverable. Such transcripts would be difficult to recover by traditional subtraction methods.

In addition to genes known to be overexpressed in prostate tumor, seventy-seven further clones were identified. Sequences of these partial cDNAs are provided in SEQ ID NO: 29 to 305. Most of these clones had no significant homology to database sequences. Exceptions were JPTPN23 (SEQ ID NO: 231; similarity to pig valosin-containing protein), JPTPN30 (SEQ ID NO: 234; similarity to rat mRNA for proteasome subunit), JPTPN45 (SEQ ID NO: 243; similarity to rat *norvegicus* cytosolic NADP-dependent isocitrate dehydrogenase), JPTPN46 (SEQ ID NO: 244; similarity to human subclone H8 4 d4 DNA sequence), JP1D6 (SEQ ID NO: 265; similarity to *G. gallus* dynein light chain-A), JP8D6 (SEQ ID NO: 288; similarity to human BAC clone RG016J04), JP8F5 (SEQ ID NO: 289; similarity to human subclone H8 3 b5 DNA sequence), and JP8E9 (SEQ ID NO: 299; similarity to human Alu sequence).

Additional studies using the PCR-based subtraction library consisting of a prostate tumor pool subtracted against a normal prostate pool (referred to as PT-PN PCR subtraction) yielded three additional clones. Comparison of the cDNA sequences of these clones with the most

recent release of GenBank revealed no significant homologies to the two clones referred to as P715P and P767P (SEQ ID NO: 312 and 314). The remaining clone was found to show some homology to the known gene KIAA0056 (SEQ ID NO: 318). Using microarray analysis to measure mRNA expression levels in various tissues, all three clones were found to be over-expressed in prostate tumors and BPH tissues. Specifically, clone P715P was over-expressed in most prostate tumors and BPH tissues by a factor of three or greater, with elevated expression seen in the majority of normal prostate samples and in fetal tissue, but negative to low expression in all other normal tissues. Clone P767P was over-expressed in several prostate tumors and BPH tissues, with moderate expression levels in half of the normal prostate samples, and background to low expression in all other normal tissues tested.

Further analysis, by microarray as described above, of the PT-PN PCR subtraction library and of a DNA subtraction library containing cDNA from prostate tumor subtracted with a pool of normal tissue cDNAs, led to the isolation of 27 additional clones (SEQ ID NO: 340-365 and 381) which were determined to be over-expressed in prostate tumor. The clones of SEQ ID NO: 341, 342, 345, 347, 348, 349, 351, 355-359, 361, 362 and 364 were also found to be expressed in normal prostate. Expression of all 26 clones in a variety of normal tissues was found to be low or undetectable, with the exception of P544S (SEQ ID NO: 356) which was found to be expressed in small intestine. Of the 26 clones, 10 (SEQ ID NO: 340-349) were found to show some homology to previously identified sequences. No significant homologies were found to the clones of SEQ ID NO: 350, 351 and 353-365.

Further studies on the clone of SEQ ID NO: 352 (referred to as P790P) led to the isolation of the full-length cDNA sequence of SEQ ID NO: 526. The corresponding predicted amino acid is provided in SEQ ID NO: 527. Data from two quantitative PCR experiments indicated that P790P is over-expressed in 11/15 tested prostate tumor samples and is expressed at low levels in spinal cord, with no expression being seen in all other normal samples tested. Data from further PCR experiments and microarray experiments showed over-expression in normal prostate and prostate tumor with little or no expression in other tissues tested. P790P was subsequently found to show significant homology to a previously identified G-protein coupled prostate tissue receptor.

EXAMPLE 6

PEPTIDE PRIMING OF MICE AND PROPAGATION OF CTL LINES

5 6.1. This Example illustrates the preparation of a CTL cell line specific for cells expressing the P502S gene.

Mice expressing the transgene for human HLA A2Kb (provided by Dr L. Sherman, The Scripps Research Institute, La Jolla, CA) were immunized with P2S#12 peptide (VLGWVAEL; SEQ ID NO: 306), which is derived from the P502S gene (also referred to herein as J1-17, SEQ ID
10 NO: 8), as described by Theobald et al., *Proc. Natl. Acad. Sci. USA* 92:11993-11997, 1995 with the following modifications. Mice were immunized with 100µg of P2S#12 and 120µg of an I-A^b binding peptide derived from hepatitis B Virus protein emulsified in incomplete Freund's adjuvant. Three weeks later these mice were sacrificed and using a nylon mesh single cell suspensions prepared. Cells were then resuspended at 6×10^6 cells/ml in complete media (RPMI-1640; Gibco
15 BRL, Gaithersburg, MD) containing 10% FCS, 2mM Glutamine (Gibco BRL), sodium pyruvate (Gibco BRL), non-essential amino acids (Gibco BRL), 2×10^{-5} M 2-mercaptoethanol, 50U/ml penicillin and streptomycin, and cultured in the presence of irradiated (3000 rads) P2S#12-pulsed (5mg/ml P2S#12 and 10mg/ml β2-microglobulin) LPS blasts (A2 transgenic spleens cells cultured in the presence of 7µg/ml dextran sulfate and 25µg/ml LPS for 3 days). Six days later, cells ($5 \times$
20 10^5 /ml) were restimulated with 2.5×10^6 /ml peptide pulsed irradiated (20,000 rads) EL4A2Kb cells (Sherman et al, *Science* 258:815-818, 1992) and 3×10^6 /ml A2 transgenic spleen feeder cells. Cells were cultured in the presence of 20U/ml IL-2. Cells continued to be restimulated on a weekly basis as described, in preparation for cloning the line.

P2S#12 line was cloned by limiting dilution analysis with peptide pulsed EL4 A2Kb
25 tumor cells (1×10^4 cells/ well) as stimulators and A2 transgenic spleen cells as feeders (5×10^5 cells/ well) grown in the presence of 30U/ml IL-2. On day 14, cells were restimulated as before. On day 21, clones that were growing were isolated and maintained in culture. Several of these clones demonstrated significantly higher reactivity (lysis) against human fibroblasts (HLA A2Kb expressing) transduced with P502S than against control fibroblasts. An example is presented in
30 Figure 1.

This data indicates that P2S #12 represents a naturally processed epitope of the P502S protein that is expressed in the context of the human HLA A2Kb molecule.

6.2. This Example illustrates the preparation of murine CTL lines and CTL clones specific for cells expressing the P501S gene.

This series of experiments were performed similarly to that described above. Mice were immunized with the P1S#10 peptide (SEQ ID NO: 337), which is derived from the P501S gene (also referred to herein as L1-12, SEQ ID NO: 110). The P1S#10 peptide was derived by analysis of the predicted polypeptide sequence for P501S for potential HLA-A2 binding sequences as defined by published HLA-A2 binding motifs (Parker, KC, *et al*, *J. Immunol.*, 152:163, 1994). P1S#10 peptide was synthesized as described in Example 4, and empirically tested for HLA-A2 binding using a T cell based competition assay. Predicted A2 binding peptides were tested for their ability to compete HLA-A2 specific peptide presentation to an HLA-A2 restricted CTL clone (D150M58), which is specific for the HLA-A2 binding influenza matrix peptide fluM58. D150M58 CTL secretes TNF in response to self-presentation of peptide fluM58. In the competition assay, test peptides at 100-200 µg/ml were added to cultures of D150M58 CTL in order to bind HLA-A2 on the CTL. After thirty minutes, CTL cultured with test peptides, or control peptides, were tested for their antigen dose response to the fluM58 peptide in a standard TNF bioassay. As shown in Figure 3, peptide P1S#10 competes HLA-A2 restricted presentation of fluM58, demonstrating that peptide P1S#10 binds HLA-A2.

Mice expressing the transgene for human HLA A2Kb were immunized as described by Theobald *et al.* (*Proc. Natl. Acad. Sci. USA* 92:11993-11997, 1995) with the following modifications. Mice were immunized with 62.5µg of P1S #10 and 120µg of an I-A^b binding peptide derived from Hepatitis B Virus protein emulsified in incomplete Freund's adjuvant. Three weeks later these mice were sacrificed and single cell suspensions prepared using a nylon mesh. Cells were then resuspended at 6×10^6 cells/ml in complete media (as described above) and cultured in the presence of irradiated (3000 rads) P1S#10-pulsed (2µg/ml P1S#10 and 10mg/ml β2-microglobulin) LPS blasts (A2 transgenic spleens cells cultured in the presence of 7µg/ml dextran sulfate and 25µg/ml LPS for 3 days). Six days later cells (5×10^5 /ml) were restimulated with 2.5×10^6 /ml peptide-pulsed irradiated (20,000 rads) EL4A2Kb cells, as described above, and 3×10^6 /ml A2 transgenic spleen feeder cells. Cells were cultured in the presence of 20 U/ml IL-2. Cells were restimulated on a weekly basis in preparation for cloning. After three rounds of *in vitro* stimulations, one line was generated that recognized P1S#10-pulsed Jurkat A2Kb targets and P501S-transduced Jurkat targets as shown in Figure 4.

A P1S#10-specific CTL line was cloned by limiting dilution analysis with peptide pulsed EL4 A2Kb tumor cells (1×10^4 cells/ well) as stimulators and A2 transgenic spleen cells as feeders (5×10^5 cells/ well) grown in the presence of 30U/ml IL-2. On day 14, cells were restimulated as before. On day 21, viable clones were isolated and maintained in culture. As shown in Figure 5, five of these clones demonstrated specific cytolytic reactivity against P501S-transduced Jurkat A2Kb targets. This data indicates that P1S#10 represents a naturally processed epitope of the P501S protein that is expressed in the context of the human HLA-A2.1 molecule.

EXAMPLE 7

PRIMING OF CTL *IN VIVO* USING NAKED DNA IMMUNIZATION WITH A PROSTATE ANTIGEN

The prostate-specific antigen L1-12, as described above, is also referred to as P501S. HLA A2Kb Tg mice (provided by Dr L. Sherman, The Scripps Research Institute, La Jolla, CA) were immunized with 100 μ g P501S in the vector VR1012 either intramuscularly or intradermally. The mice were immunized three times, with a two week interval between immunizations. Two weeks after the last immunization, immune spleen cells were cultured with Jurkat A2Kb-P501S transduced stimulator cells. CTL lines were stimulated weekly. After two weeks of *in vitro* stimulation, CTL activity was assessed against P501S transduced targets. Two out of 8 mice developed strong anti-P501S CTL responses. These results demonstrate that P501S contains at least one naturally processed HLA-A2-restricted CTL epitope.

EXAMPLE 8

ABILITY OF HUMAN T CELLS TO RECOGNIZE PROSTATE-SPECIFIC POLYPEPTIDES

This Example illustrates the ability of T cells specific for a prostate tumor polypeptide to recognize human tumor.

Human CD8⁺ T cells were primed *in vitro* to the P2S-12 peptide (SEQ ID NO: 306) derived from P502S (also referred to as J1-17) using dendritic cells according to the protocol of Van Tsai et al. (*Critical Reviews in Immunology* 18:65-75, 1998). The resulting CD8⁺ T cell microcultures were tested for their ability to recognize the P2S-12 peptide presented by autologous fibroblasts or fibroblasts which were transduced to express the P502S gene in a γ -interferon

ELISPOT assay (*see* Lalvani et al., *J. Exp. Med.* 186:859-865, 1997). Briefly, titrating numbers of T cells were assayed in duplicate on 10^4 fibroblasts in the presence of 3 $\mu\text{g/ml}$ human β_2 -microglobulin and 1 $\mu\text{g/ml}$ P2S-12 peptide or control E75 peptide. In addition, T cells were simultaneously assayed on autologous fibroblasts transduced with the P502S gene or as a control, fibroblasts transduced with HER-2/*neu*. Prior to the assay, the fibroblasts were treated with 10 ng/ml γ -interferon for 48 hours to upregulate class I MHC expression. One of the microcultures (#5) demonstrated strong recognition of both peptide pulsed fibroblasts as well as transduced fibroblasts in a γ -interferon ELISPOT assay. Figure 2A demonstrates that there was a strong increase in the number of γ -interferon spots with increasing numbers of T cells on fibroblasts pulsed with the P2S-12 peptide (solid bars) but not with the control E75 peptide (open bars). This shows the ability of these T cells to specifically recognize the P2S-12 peptide. As shown in Figure 2B, this microculture also demonstrated an increase in the number of γ -interferon spots with increasing numbers of T cells on fibroblasts transduced to express the P502S gene but not the HER-2/*neu* gene. These results provide additional confirmatory evidence that the P2S-12 peptide is a naturally processed epitope of the P502S protein. Furthermore, this also demonstrates that there exists in the human T cell repertoire, high affinity T cells which are capable of recognizing this epitope. These T cells should also be capable of recognizing human tumors which express the P502S gene.

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EXAMPLE 9

ELICITATION OF PROSTATE ANTIGEN-SPECIFIC CTL RESPONSES
IN HUMAN BLOOD

This Example illustrates the ability of a prostate-specific antigen to elicit a CTL response in blood of normal humans.

Autologous dendritic cells (DC) were differentiated from monocyte cultures derived from PBMC of normal donors by growth for five days in RPMI medium containing 10% human serum, 50 ng/ml GM-CSF and 30 ng/ml IL-4. Following culture, DC were infected overnight with recombinant P501S-expressing vaccinia virus at an M.O.I. of 5 and matured for 8 hours by the addition of 2 micrograms/ml CD40 ligand. Virus was inactivated by UV irradiation, CD8⁺ cells were isolated by positive selection using magnetic beads, and priming cultures were initiated in 24-well plates. Following five stimulation cycles using autologous fibroblasts retrovirally transduced

to express P501S and CD80, CD8+ lines were identified that specifically produced interferon-gamma when stimulated with autologous P501S-transduced fibroblasts. The P501S-specific activity of cell line 3A-1 could be maintained following additional stimulation cycles on autologous B-LCL transduced with P501S. Line 3A-1 was shown to specifically recognize autologous B-LCL transduced to express P501S, but not EGFP-transduced autologous B-LCL, as measured by cytotoxicity assays (^{51}Cr release) and interferon-gamma production (Interferon-gamma Elispot; *see* above and Lalvani et al., *J. Exp. Med.* 186:859-865, 1997). The results of these assays are presented in Figures 6A and 6B.

EXAMPLE 10

IDENTIFICATION OF A NATURALLY PROCESSED CTL EPIOTOPE CONTAINED WITHIN A PROSTATE-SPECIFIC ANTIGEN

The 9-mer peptide p5 (SEQ ID NO: 338) was derived from the P703P antigen (also referred to as P20). The p5 peptide is immunogenic in human HLA-A2 donors and is a naturally processed epitope. Antigen specific human CD8+ T cells can be primed following repeated *in vitro* stimulations with monocytes pulsed with p5 peptide. These CTL specifically recognize p5-pulsed and P703P-transduced target cells in both ELISPOT (as described above) and chromium release assays. Additionally, immunization of HLA-A2Kb transgenic mice with p5 leads to the generation of CTL lines which recognize a variety of HLA-A2Kb or HLA-A2 transduced target cells expressing P703P.

Initial studies demonstrating that p5 is a naturally processed epitope were done using HLA-A2Kb transgenic mice. HLA-A2Kb transgenic mice were immunized subcutaneously in the footpad with 100 μg of p5 peptide together with 140 μg of hepatitis B virus core peptide (a Th peptide) in Freund's incomplete adjuvant. Three weeks post immunization, spleen cells from immunized mice were stimulated *in vitro* with peptide-pulsed LPS blasts. CTL activity was assessed by chromium release assay five days after primary *in vitro* stimulation. Retrovirally transduced cells expressing the control antigen P703P and HLA-A2Kb were used as targets. CTL lines that specifically recognized both p5-pulsed targets as well as P703P-expressing targets were identified.

Human *in vitro* priming experiments demonstrated that the p5 peptide is immunogenic in humans. Dendritic cells (DC) were differentiated from monocyte cultures derived

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Using *in vitro* whole-gene priming with P501S-vaccinia infected DC (see, for example, Yee et al, *The Journal of Immunology*, 157(9):4079-86, 1996), human CTL lines were derived that specifically recognize autologous fibroblasts transduced with P501S (also known as L1-12), as determined by interferon- γ ELISPOT analysis as described above. Using a panel of HLA-mismatched B-LCL lines transduced with P501S, these CTL lines were shown to be likely restricted to HLAB class I allele. Specifically, dendritic cells (DC) were differentiated from monocyte cultures derived from PBMC of normal human donors by growing for five days in RPMI medium containing 10% human serum, 50 ng/ml human GM-CSF and 30 ng/ml human IL-4. Following culture, DC were infected overnight with recombinant P501S vaccinia virus at a multiplicity of infection (M.O.I) of five, and matured overnight by the addition of 3 μ g/ml CD40 ligand. Virus was inactivated by UV irradiation. CD8⁺ T cells were isolated using a magnetic bead system, and priming cultures were initiated using standard culture techniques. Cultures were restimulated every 7-10 days using autologous primary fibroblasts retrovirally transduced with P501S and CD80. Following four stimulation cycles, CD8⁺ T cell lines were identified that specifically produced interferon- γ when stimulated with P501S and CD80-transduced autologous fibroblasts. A panel of HLA-mismatched B-LCL lines transduced with P501S were generated to define the restriction allele of the response. By measuring interferon- γ in an ELISPOT assay, the P501S specific response was shown to be likely restricted by HLA B alleles. These results demonstrate that a CD8⁺ CTL response to P501S can be elicited.

To identify the epitope(s) recognized, cDNA encoding P501S was fragmented by various restriction digests, and sub-cloned into the retroviral expression vector pBIB-KS. Retroviral supernatants were generated by transfection of the helper packaging line Phoenix-Ampho. Supernatants were then used to transduce Jurkat/A2Kb cells for CTL screening. CTL were screened in IFN- γ ELISPOT assays against these A2Kb targets transduced with the "library" of P501S fragments. Initial positive fragments P501S/H3 and P501S/F2 were sequenced and found to encode amino acids 106-553 and amino acids 136-547, respectively, of SEQ ID NO: 113. A truncation of H3 was made to encode amino acid residues 106-351 of SEQ ID NO: 113, which was unable to stimulate the CTL, thus localizing the epitope to amino acid residues 351-547. Additional fragments encoding amino acids 1-472 (Fragment A) and amino acids 1-351 (Fragment B) were also constructed. Fragment A but not Fragment B stimulated the CTL thus localizing the epitope to amino acid residues 351-472. Overlapping 20-mer and 18-mer peptides representing this region were tested by pulsing Jurkat/A2Kb cells versus CTL in an IFN- γ assay. Only peptides

P501S-369(20) and P501S-369(18) stimulated the CTL. Nine-mer and 10-mer peptides representing this region were synthesized and similarly tested. Peptide P501S-370 (SEQ ID NO: 539) was the minimal 9-mer giving a strong response. Peptide P501S-376 (SEQ ID NO: 540) also gave a weak response, suggesting that it might represent a cross-reactive epitope.

5 In subsequent studies, the ability of primary human B cells transduced with P501S to prime MHC class I-restricted, P501S-specific, autologous CD8 T cells was examined. Primary B cells were derived from PBMC of a homozygous HLA-A2 donor by culture in CD40 ligand and IL-4, transduced at high frequency with recombinant P501S in the vector pBIB, and selected with blastocidin-S. For *in vitro* priming, purified CD8+ T cells were cultured with autologous CD40
10 ligand + IL-4 derived, P501S-transduced B cells in a 96-well microculture format. These CTL microcultures were re-stimulated with P501S-transduced B cells and then assayed for specificity. Following this initial screen, microcultures with significant signal above background were cloned on autologous EBV-transformed B cells (BLCL), also transduced with P501S. Using IFN-gamma ELISPOT for detection, several of these CD8 T cell clones were found to be specific for P501S, as
15 demonstrated by reactivity to BLCL/P501S but not BLCL transduced with control antigen. It was further demonstrated that the anti-P501S CD8 T cell specificity is HLA-A2-restricted. First, antibody blocking experiments with anti-HLA-A,B,C monoclonal antibody (W6.32), anti-HLA-B,C monoclonal antibody (B1.23.2) and a control monoclonal antibody showed that only the anti-HLA-A,B,C antibody blocked recognition of P501S-expressing autologous BLCL. Secondly, the anti-
20 P501S CTL also recognized an HLA-A2 matched, heterologous BLCL transduced with P501S, but not the corresponding EGFP transduced control BLCL.

EXAMPLE 13

IDENTIFICATION OF PROSTATE-SPECIFIC ANTIGENS BY MICROARRAY ANALYSIS

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This Example describes the isolation of certain prostate-specific polypeptides from a prostate tumor cDNA library.

A human prostate tumor cDNA expression library as described above was screened using microarray analysis to identify clones that display at least a three fold over-expression in
30 prostate tumor and/or normal prostate tissue, as compared to non-prostate normal tissues (not including testis). 372 clones were identified, and 319 were successfully sequenced. Table I presents a summary of these clones, which are shown in SEQ ID NOs:385-400. Of these sequences

SEQ ID NOs:386, 389, 390 and 392 correspond to novel genes, and SEQ ID NOs: 393 and 396 correspond to previously identified sequences. The others (SEQ ID NOs:385, 387, 388, 391, 394, 395 and 397-400) correspond to known sequences, as shown in Table I.

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Table I
Summary of Prostate Tumor Antigens

Known Genes	Previously Identified Genes	Novel Genes
T-cell gamma chain	P504S	23379 (SEQ ID NO:389)
Kallikrein	P1000C	23399 (SEQ ID NO:392)
Vector	P501S	23320 (SEQ ID NO:386)
CGI-82 protein mRNA (23319; SEQ ID NO:385)	P503S	23381 (SEQ ID NO:390)
PSA	P510S	
Ald. 6 Dehyd.	P784P	
L-iditol-2 dehydrogenase (23376; SEQ ID NO:388)	P502S	
Ets transcription factor PDEF (22672; SEQ ID NO:398)	P706P	
hTGR (22678; SEQ ID NO:399)	19142.2, bangur.seq (22621; SEQ ID NO:396)	
KIAA0295(22685; SEQ ID NO:400)	5566.1 Wang (23404; SEQ ID NO:393)	
Prostatic Acid Phosphatase(22655; SEQ ID NO:397)	P712P	
transglutaminase (22611; SEQ ID NO:395)	P778P	
HDLBP (23508; SEQ ID NO:394)		
CGI-69 Protein(23367; SEQ ID NO:387)		
KIAA0122(23383; SEQ ID NO:391)		
TEEG		

CGI-82 showed 4.06 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 43% of prostate tumors, 25% normal prostate, not detected in other normal tissues tested. L-iditol-2 dehydrogenase showed 4.94 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 90% of prostate tumors, 100% of normal prostate, and not detected in other normal tissues tested. Its transcription factor PDEF showed 5.55 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 47% prostate tumors, 25% normal prostate and not detected in other normal tissues tested. hTGR1 showed 9.11 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 63% of prostate tumors and is not detected in normal tissues tested including normal prostate. KIAA0295 showed 5.59 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 47% of prostate tumors, low to undetectable in normal tissues tested including normal prostate tissues. Prostatic acid phosphatase showed 9.14 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 67% of prostate tumors, 50% of normal prostate, and not detected in other normal tissues tested. Transglutaminase showed 14.84 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 30% of prostate tumors, 50% of normal prostate, and is not detected in other normal tissues tested. High density lipoprotein binding protein (HDLBP) showed 28.06 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 97% of prostate tumors, 75% of normal prostate, and is undetectable in all other normal tissues tested. CGI-69 showed 3.56 fold over-expression in prostate tissues as compared to other normal tissues tested. It is a low abundant gene, detected in more than 90% of prostate tumors, and in 75% normal prostate tissues. The expression of this gene in normal tissues was very low. KIAA0122 showed 4.24 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 57% of prostate tumors, it was undetectable in all normal tissues tested including normal prostate tissues. 19142.2 bangur showed 23.25 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 97% of prostate tumors and 100% of normal prostate. It was undetectable in other normal tissues tested. 5566.1 Wang showed 3.31 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 97% of prostate tumors, 75% normal prostate and was also over-expressed in normal bone marrow, pancreas, and activated PBMC. Novel clone 23379 showed 4.86 fold over-expression in prostate tissues as compared to other normal tissues tested. It was detectable in 97%

of prostate tumors and 75% normal prostate and is undetectable in all other normal tissues tested. Novel clone 23399 showed 4.09 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 27% of prostate tumors and was undetectable in all normal tissues tested including normal prostate tissues. Novel clone 23320 showed 3.15 fold over-expression in prostate tissues as compared to other normal tissues tested. It was detectable in all prostate tumors and 50% of normal prostate tissues. It was also expressed in normal colon and trachea. Other normal tissues do not express this gene at high level.

EXAMPLE 14

IDENTIFICATION OF PROSTATE-SPECIFIC ANTIGENS BY ELECTRONIC SUBTRACTION

This Example describes the use of an electronic subtraction technique to identify prostate-specific antigens.

Potential prostate-specific genes present in the GenBank human EST database were identified by electronic subtraction (similar to that described by Vasmatizis et al., *Proc. Natl. Acad. Sci. USA* 95:300-304, 1998). The sequences of EST clones (43,482) derived from various prostate libraries were obtained from the GenBank public human EST database. Each prostate EST sequence was used as a query sequence in a BLASTN (National Center for Biotechnology Information) search against the human EST database. All matches considered identical (length of matching sequence >100 base pairs, density of identical matches over this region > 70%) were grouped (aligned) together in a cluster. Clusters containing more than 200 ESTs were discarded since they probably represented repetitive elements or highly expressed genes such as those for ribosomal proteins. If two or more clusters shared common ESTs, those clusters were grouped together into a "supercluster," resulting in 4,345 prostate superclusters.

Records for the 479 human cDNA libraries represented in the GenBank release were downloaded to create a database of these cDNA library records. These 479 cDNA libraries were grouped into three groups: Plus (normal prostate and prostate tumor libraries, and breast cell line libraries, in which expression was desired), Minus (libraries from other normal adult tissues, in which expression was not desirable), and Other (libraries from fetal tissue, infant tissue, tissues found only in women, non-prostate tumors and cell lines other than prostate cell lines, in which

expression was considered to be irrelevant). A summary of these library groups is presented in Table II.

Table II

Prostate cDNA Libraries and ESTs

Library	# of Libraries	# of ESTs
Plus	25	43,482
Normal	11	18,875
Tumor	11	21,769
Cell lines	3	2,838
Minus	166	
Other	287	

Each supercluster was analyzed in terms of the ESTs within the supercluster. The tissue source of each EST clone was noted and used to classify the superclusters into four groups:

10 Type 1- EST clones found in the Plus group libraries only; no expression detected in Minus or Other group libraries; Type 2- EST clones derived from the Plus and Other group libraries only; no expression detected in the Minus group; Type 3- EST clones derived from the Plus, Minus and Other group libraries, but the number of ESTs derived from the Plus group is higher than in either the Minus or Other groups; and Type 4- EST clones derived from Plus, Minus and Other group

15 libraries, but the number derived from the Plus group is higher than the number derived from the Minus group. This analysis identified 4,345 breast clusters (see Table III). From these clusters, 3,172 EST clones were ordered from Research Genetics, Inc., and were received as frozen glycerol stocks in 96-well plates.

Table III
Prostate Cluster Summary

Type	# of Superclusters	# of ESTs Ordered
1	688	677
2	2899	2484
3	85	11
4	673	0
Total	4345	3172

The EST clone inserts were PCR-amplified using amino-linked PCR primers for Synteni microarray analysis. When more than one PCR product was obtained for a particular clone, that PCR product was not used for expression analysis. In total, 2,528 clones from the electronic subtraction method were analyzed by microarray analysis to identify electronic subtraction breast clones that had high levels of tumor vs. normal tissue mRNA. Such screens were performed using a Synteni (Palo Alto, CA) microarray, according to the manufacturer's instructions (and essentially as described by Schena et al., *Proc. Natl. Acad. Sci. USA* 93:10614-10619, 1996 and Heller et al., *Proc. Natl. Acad. Sci. USA* 94:2150-2155, 1997). Within these analyses, the clones were arrayed on the chip, which was then probed with fluorescent probes generated from normal and tumor prostate cDNA, as well as various other normal tissues. The slides were scanned and the fluorescence intensity was measured.

Clones with an expression ratio greater than 3 (*i.e.*, the level in prostate tumor and normal prostate mRNA was at least three times the level in other normal tissue mRNA) were identified as prostate tumor-specific sequences (Table IV). The sequences of these clones are provided in SEQ ID NO: 401-453, with certain novel sequences shown in SEQ ID NO: 407, 413, 416-419, 422, 426, 427 and 450.

Table IV
Prostate-tumor Specific Clones

SEQ ID NO.	Sequence Designation	Comments
401	22545	previously identified P1000C
402	22547	previously identified P704P
403	22548	known
404	22550	known
405	22551	PSA
406	22552	prostate secretory protein 94
407	22553	novel
408	22558	previously identified P509S
409	22562	glandular kallikrein
410	22565	previously identified P1000C
411	22567	PAP
412	22568	B1006C (breast tumor antigen)
413	22570	novel
414	22571	PSA
415	22572	previously identified P706P
416	22573	novel
417	22574	novel
418	22575	novel
419	22580	novel
420	22581	PAP
421	22582	prostatic secretory protein 94
422	22583	novel
423	22584	prostatic secretory protein 94
424	22585	prostatic secretory protein 94
425	22586	known
426	22587	novel
427	22588	novel
428	22589	PAP
429	22590	known
430	22591	PSA
431	22592	known
432	22593	Previously identified P777P
433	22594	T cell receptor gamma chain
434	22595	Previously identified P705P
435	22596	Previously identified P707P
436	22847	PAP
437	22848	known
438	22849	prostatic secretory protein 57
439	22851	PAP

440	22852	PAP
441	22853	PAP
442	22854	previously identified P509S
443	22855	previously identified P705P
444	22856	previously identified P774P
445	22857	PSA
446	23601	previously identified P777P
447	23602	PSA
448	23605	PSA
449	23606	PSA
450	23612	novel
451	23614	PSA
452	23618	previously identified P1000C
453	23622	previously identified P705P

EXAMPLE 15

FURTHER IDENTIFICATION OF PROSTATE-SPECIFIC ANTIGENS BY MICROARRAY
ANALYSIS

This Example describes the isolation of additional prostate-specific polypeptides from a prostate tumor cDNA library.

A human prostate tumor cDNA expression library as described above was screened using microarray analysis to identify clones that display at least a three fold over-expression in prostate tumor and/or normal prostate tissue, as compared to non-prostate normal tissues (not including testis). 142 clones were identified and sequenced. Certain of these clones are shown in SEQ ID NO: 454-467. Of these sequences, SEQ ID NO: 459-461 represent novel genes. The others (SEQ ID NO: 454-458 and 461-467) correspond to known sequences.

EXAMPLE 16

FURTHER CHARACTERIZATION OF PROSTATE-SPECIFIC ANTIGEN P710P

This Example describes the full length cloning of P710P.

The prostate cDNA library described above was screened with the P710P fragment described above. One million colonies were plated on LB/Ampicillin plates. Nylon membrane

filters were used to lift these colonies, and the cDNAs picked up by these filters were then denatured and cross-linked to the filters by UV light. The P710P fragment was radiolabeled and used to hybridize with the filters. Positive cDNA clones were selected and their cDNAs recovered and sequenced by an automatic Perkin Elmer/Applied Biosystems Division Sequencer. Four
5 sequences were obtained, and are presented in SEQ ID NO: 468-471. These sequences appear to represent different splice variants of the P710P gene.

EXAMPLE 17

PROTEIN EXPRESSION OF THE PROSTATE-SPECIFIC ANTIGEN P501S

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This example describes the expression and purification of the prostate-specific antigen P501S in *E. coli*, baculovirus and mammalian cells.

a) Expression in *E. coli*

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Expression of the full-length form of P501S was attempted by first cloning P501S without the leader sequence (amino acids 36-553 of SEQ ID NO: 113) downstream of the first 30 amino acids of the *M. tuberculosis* antigen Ra12 (SEQ ID NO: 484) in pET17b. Specifically, P501S DNA was used to perform PCR using the primers AW025 (SEQ ID NO: 485) and AW003 (SEQ ID NO: 486). AW025 is a sense cloning primer that contains a HindIII site. AW003 is an
20 antisense cloning primer that contains an EcoRI site. DNA amplification was performed using 5 µl 10X Pfu buffer, 1 µl 20 mM dNTPs, 1 µl each of the PCR primers at 10 µM concentration, 40 µl water, 1 µl Pfu DNA polymerase (Stratagene, La Jolla, CA) and 1 µl DNA at 100 ng/µl. Denaturation at 95°C was performed for 30 sec, followed by 10 cycles of 95°C for 30 sec, 60°C for 1 min and by 72°C for 3 min. 20 cycles of 95°C for 30 sec, 65°C for 1 min and by 72°C for 3 min,
25 and lastly by 1 cycle of 72°C for 10 min. The PCR product was cloned to Ra12m/pET17b using HindIII and EcoRI. The sequence of the resulting fusion construct (referred to as Ra12-P501S-F) was confirmed by DNA sequencing.

The fusion construct was transformed into BL21(DE3)pLysE, pLysS and CodonPlus *E. coli* (Stratagene) and grown overnight in LB broth with kanamycin. The resulting culture was
30 induced with IPTG. Protein was transferred to PVDF membrane and blocked with 5% non-fat milk (in PBS-Tween buffer), washed three times and incubated with mouse anti-His tag antibody (Clontech) for 1 hour. The membrane was washed 3 times and probed with HRP-Protein A

(Zymed) for 30 min. Finally, the membrane was washed 3 times and developed with ECL (Amersham). No expression was detected by Western blot. Similarly, no expression was detected by Western blot when the Ra12-P501S-F fusion was used for expression in BL21CodonPlus by CE6 phage (Invitrogen).

5 An N-terminal fragment of P501S (amino acids 36-325 of SEQ ID NO: 113) was cloned down-stream of the first 30 amino acids of the *M. tuberculosis* antigen Ra12 in pET17b as follows. P501S DNA was used to perform PCR using the primers AW025 (SEQ ID NO: 485) and AW027 (SEQ ID NO: 487). AW027 is an antisense cloning primer that contains an EcoRI site and a stop codon. DNA amplification was performed essentially as described above. The resulting PCR
10 product was cloned to Ra12 in pET17b at the HindIII and EcoRI sites. The fusion construct (referred to as Ra12-P501S-N) was confirmed by DNA sequencing.

 The Ra12-P501S-N fusion construct was used for expression in BL21(DE3)pLysE, pLysS and CodonPlus, essentially as described above. Using Western blot analysis, protein bands were observed at the expected molecular weight of 36 kDa. Some high molecular weight bands
15 were also observed, probably due to aggregation of the recombinant protein. No expression was detected by Western blot when the Ra12-P501S-F fusion was used for expression in BL21CodonPlus by CE6 phage.

 A fusion construct comprising a C-terminal portion of P501S (amino acids 257-553 of SEQ ID NO: 113) located down-stream of the first 30 amino acids of the *M. tuberculosis* antigen
20 Ra12 (SEQ ID NO: 484) was prepared as follows. P501S DNA was used to perform PCR using the primers AW026 (SEQ ID NO: 488) and AW003 (SEQ ID NO: 486). AW026 is a sense cloning primer that contains a HindIII site. DNA amplification was performed essentially as described above. The resulting PCR product was cloned to Ra12 in pET17b at the HindIII and EcoRI sites. The sequence for the fusion construct (referred to as Ra12-P501S-C) was confirmed.

25 The Ra12-P501S-C fusion construct was used for expression in BL21(DE3)pLysE, pLysS and CodonPlus, as described above. A small amount of protein was detected by Western blot, with some molecular weight aggregates also being observed. Expression was also detected by Western blot when the Ra12-P501S-C fusion was used for expression in BL21CodonPlus induced by CE6 phage.

b) Expression of P501S in Baculovirus

The Bac-to-Bac baculovirus expression system (BRL Life Technologies, Inc.) was used to express P501S protein in insect cells. Full-length P501S (SEQ ID NO: 113) was amplified by PCR and cloned into the XbaI site of the donor plasmid pFastBacI. The recombinant bacmid and baculovirus were prepared according to the manufacturer's instructions. The recombinant baculovirus was amplified in Sf9 cells and the high titer viral stocks were utilized to infect High Five cells (Invitrogen) to make the recombinant protein. The identity of the full-length protein was confirmed by N-terminal sequencing of the recombinant protein and by Western blot analysis (Figure 7). Specifically, 0.6 million High Five cells in 6-well plates were infected with either the unrelated control virus BV/ECD_PD (lane 2), with recombinant baculovirus for P501S at different amounts or MOIs (lanes 4-8), or were uninfected (lane 3). Cell lysates were run on SDS-PAGE under reducing conditions and analyzed by Western blot with the anti-P501S monoclonal antibody P501S-10E3-G4D3 (prepared as described below). Lane 1 is the biotinylated protein molecular weight marker (BioLabs).

The localization of recombinant P501S in the insect cells was investigated as follows. The insect cells overexpressing P501S were fractionated into fractions of nucleus, mitochondria, membrane and cytosol. Equal amounts of protein from each fraction were analyzed by Western blot with a monoclonal antibody against P501S. Due to the scheme of fractionation, both nucleus and mitochondria fractions contain some plasma membrane components. However, the membrane fraction is basically free from mitochondria and nucleus. P501S was found to be present in all fractions that contain the membrane component, suggesting that P501S may be associated with plasma membrane of the insect cells expressing the recombinant protein.

c) Expression of P501S in mammalian cells

Full-length P501S (553AA) was cloned into various mammalian expression vectors, including pCEP4 (Invitrogen), pVR1012 (Vical, San Diego, CA) and a modified form of the retroviral vector pBMN, referred to as pBIB. Transfection of P501S/pCEP4 and P501S/pVR1012 into HEK293 fibroblasts was carried out using the Fugene transfection reagent (Boehringer Mannheim). Briefly, 2 ul of Fugene reagent was diluted into 100 ul of serum-free media and incubated at room temperature for 5-10 min. This mixture was added to 1 ug of P501S plasmid DNA, mixed briefly and incubated for 30 minutes at room temperature. The Fugene/DNA mixture

was added to cells and incubated for 24-48 hours. Expression of recombinant P501S in transfected HEK293 fibroblasts was detected by means of Western blot employing a monoclonal antibody to P501S.

Transfection of p501S/pCEP4 into CHO-K cells (American Type Culture Collection, Rockville, MD) was carried out using GenePorter transfection reagent (Gene Therapy Systems, San Diego, CA). Briefly, 15 µl of GenePorter was diluted in 500 µl of serum-free media and incubated at room temperature for 10 min. The GenePorter/media mixture was added to 2 µg of plasmid DNA that was diluted in 500 µl of serum-free media, mixed briefly and incubated for 30 min at room temperature. CHO-K cells were rinsed in PBS to remove serum proteins, and the GenePorter/DNA mix was added and incubated for 5 hours. The transfected cells were then fed an equal volume of 2x media and incubated for 24-48 hours.

FACS analysis of P501S transiently infected CHO-K cells, demonstrated surface expression of P501S. Expression was detected using rabbit polyclonal antisera raised against a P501S peptide, as described below. Flow cytometric analysis was performed using a FaCScan (Becton Dickinson), and the data were analyzed using the Cell Quest program.

EXAMPLE 18

PREPARATION AND CHARACTERIZATION OF ANTIBODIES AGAINST PROSTATE-SPECIFIC POLYPEPTIDES

20 a) Preparation and Characterization of Antibodies against P501S

A murine monoclonal antibody directed against the carboxy-terminus of the prostate-specific antigen P501S was prepared as follows.

A truncated fragment of P501S (amino acids 355-526 of SEQ ID NO: 113) was generated and cloned into the pET28b vector (Novagen) and expressed in *E. coli* as a thioredoxin fusion protein with a histidine tag. The trx-P501S fusion protein was purified by nickel chromatography, digested with thrombin to remove the trx fragment and further purified by an acid precipitation procedure followed by reverse phase HPLC.

Mice were immunized with truncated P501S protein. Serum bleeds from mice that potentially contained anti-P501S polyclonal sera were tested for P501S-specific reactivity using ELISA assays with purified P501S and trx-P501S proteins. Serum bleeds that appeared to react specifically with P501S were then screened for P501S reactivity by Western analysis. Mice that contained a P501S-specific antibody component were sacrificed and spleen cells were used to

generate anti-P501S antibody producing hybridomas using standard techniques. Hybridoma supernatants were tested for P501S-specific reactivity initially by ELISA, and subsequently by FACS analysis of reactivity with P501S transduced cells. Based on these results, a monoclonal hybridoma referred to as 10E3 was chosen for further subcloning. A number of subclones were generated, tested for specific reactivity to P501S using ELISA and typed for IgG isotype. The results of this analysis are shown below in Table V. Of the 16 subclones tested, the monoclonal antibody 10E3-G4-D3 was selected for further study.

Table V

Isotype analysis of murine anti-P501S monoclonal antibodies

Hybridoma clone	Isotype	Estimated [Ig] in supernatant (µg/ml)
4D11	IgG1	14.6
1G1	IgG1	0.6
4F6	IgG1	72
4H5	IgG1	13.8
4H5-E12	IgG1	10.7
4H5-EH2	IgG1	9.2
4H5-H2-A10	IgG1	10
4H5-H2-A3	IgG1	12.8
4H5-H2-A10-G6	IgG1	13.6
4H5-H2-B11	IgG1	12.3
10E3	IgG2a	3.4
10E3-D4	IgG2a	3.8
10E3-D4-G3	IgG2a	9.5
10E3-D4-G6	IgG2a	10.4
10E3-E7	IgG2a	6.5
8H12	IgG2a	0.6

The specificity of 10E3-G4-D3 for P501S was examined by FACS analysis.

Specifically, cells were fixed (2% formaldehyde, 10 minutes), permeabilized (0.1% saponin, 10 minutes) and stained with 10E3-G4-D3 at 0.5 – 1 µg/ml, followed by incubation with a secondary, FITC-conjugated goat anti-mouse Ig antibody (Pharmingen, San Diego, CA). Cells were then analyzed for FITC fluorescence using an Excalibur fluorescence activated cell sorter. For FACS analysis of transduced cells, B-LCL were retrovirally transduced with P501S. For analysis of infected cells, B-LCL were infected with a vaccinia vector that expresses P501S. To demonstrate

specificity in these assays, B-LCL transduced with a different antigen (P703P) and uninfected B-LCL vectors were utilized. 10E3-G4-D3 was shown to bind with P501S-transduced B-LCL and also with P501S-infected B-LCL, but not with either uninfected cells or P703P-transduced cells.

To determine whether the epitope recognized by 10E3-G4-D3 was found on the surface or in an intracellular compartment of cells, B-LCL were transduced with P501S or HLA-B8 as a control antigen and either fixed and permeabilized as described above or directly stained with 10E3-G4-D3 and analyzed as above. Specific recognition of P501S by 10E3-G4-D3 was found to require permeabilization, suggesting that the epitope recognized by this antibody is intracellular.

The reactivity of 10E3-G4-D3 with the three prostate tumor cell lines Lncap, PC-3 and DU-145, which are known to express high, medium and very low levels of P501S, respectively, was examined by permeabilizing the cells and treating them as described above. Higher reactivity of 10E3-G4-D3 was seen with Lncap than with PC-3, which in turn showed higher reactivity than DU-145. These results are in agreement with the real time PCR and demonstrate that the antibody specifically recognizes P501S in these tumor cell lines and that the epitope recognized in prostate tumor cell lines is also intracellular.

Specificity of 10E3-G4-D3 for P501S was also demonstrated by Western blot analysis. Lysates from the prostate tumor cell lines Lncap, DU-145 and PC-3, from P501S-transiently transfected HEK293 cells, and from non-transfected HEK293 cells were generated. Western blot analysis of these lysates with 10E3-G4-D3 revealed a 46 kDa immunoreactive band in Lncap, PC-3 and P501S-transfected HEK cells, but not in DU-145 cells or non-transfected HEK293 cells. P501S mRNA expression is consistent with these results since semi-quantitative PCR analysis revealed that P501S mRNA is expressed in Lncap, to a lesser but detectable level in PC-3 and not at all in DU-145 cells. Bacterially expressed and purified recombinant P501S (referred to as P501SStr2) was recognized by 10E3-G4-D3 (24 kDa), as was full-length P501S that was transiently expressed in HEK293 cells using either the expression vector VR1012 or pCEP4. Although the predicted molecular weight of P501S is 60.5 kDa, both transfected and "native" P501S run at a slightly lower mobility due to its hydrophobic nature.

Immunohistochemical analysis was performed on prostate tumor and a panel of normal tissue sections (prostate, adrenal, breast, cervix, colon, duodenum, gall bladder, ileum, kidney, ovary, pancreas, parotid gland, skeletal muscle, spleen and testis). Tissue samples were fixed in formalin solution for 24 hours and embedded in paraffin before being sliced into 10 micron sections. Tissue sections were permeabilized and incubated with 10E3-G4-D3 antibody for 1 hr.

HRP-labeled anti-mouse followed by incubation with DAB chromogen was used to visualize P501S immunoreactivity. P501S was found to be highly expressed in both normal prostate and prostate tumor tissue but was not detected in any of the other tissues tested.

To identify the epitope recognized by 10E3-G4-D3, an epitope mapping approach was pursued. A series of 13 overlapping 20-21 mers (5 amino acid overlap; SEQ ID NO: 489-501) was synthesized that spanned the fragment of P501S used to generate 10E3-G4-D3. Flat bottom 96 well microtiter plates were coated with either the peptides or the P501S fragment used to immunize mice, at 1 microgram/ml for 2 hours at 37 °C. Wells were then aspirated and blocked with phosphate buffered saline containing 1% (w/v) BSA for 2 hours at room temperature, and subsequently washed in PBS containing 0.1% Tween 20 (PBST). Purified antibody 10E3-G4-D3 was added at 2 fold dilutions (1000 ng – 16 ng) in PBST and incubated for 30 minutes at room temperature. This was followed by washing 6 times with PBST and subsequently incubating with HRP-conjugated donkey anti-mouse IgG (H+L) Affinipure F(ab') fragment (Jackson Immunoresearch, West Grove, PA) at 1:20000 for 30 minutes. Plates were then washed and incubated for 15 minutes in tetramethyl benzidine. Reactions were stopped by the addition of 1N sulfuric acid and plates were read at 450 nm using an ELISA plate reader. As shown in Fig. 8, reactivity was seen with the peptide of SEQ ID NO: 496 (corresponding to amino acids 439-459 of P501S) and with the P501S fragment but not with the remaining peptides, demonstrating that the epitope recognized by 10E3-G4-D3 is localized to amino acids 439-459 of SEQ ID NO: 113.

In order to further evaluate the tissue specificity of P501S, multi-array immunohistochemical analysis was performed on approximately 4700 different human tissues encompassing all the major normal organs as well as neoplasias derived from these tissues. Sixty-five of these human tissue samples were of prostate origin. Tissue sections 0.6 mm in diameter were formalin-fixed and paraffin embedded. Samples were pretreated with HIER using 10 mM citrate buffer pH 6.0 and boiling for 10 min. Sections were stained with 10E3-G4-D3 and P501S immunoreactivity was visualized with HRP. All the 65 prostate tissues samples (5 normal, 55 untreated prostate tumors, 5 hormone refractory prostate tumors) were positive, showing distinct perinuclear staining. All other tissues examined were negative for P501S expression.

b) Preparation and Characterization of Antibodies against P503S

A fragment of P503S (amino acids 113-241 of SEQ ID NO: 114) was expressed and purified from bacteria essentially as described above for P501S and used to immunize both rabbits

and mice. Mouse monoclonal antibodies were isolated using standard hybridoma technology as described above. Rabbit monoclonal antibodies were isolated using Selected Lymphocyte Antibody Method (SLAM) technology at Immgenics Pharmaceuticals (Vancouver, BC, Canada). Table VI, below, lists the monoclonal antibodies that were developed against P503S.

5

Table VI

Antibody	Species
20D4	Rabbit
JA1	Rabbit
1A4	Mouse
1C3	Mouse
1C9	Mouse
1D12	Mouse
2A11	Mouse
2H9	Mouse
4H7	Mouse
8A8	Mouse
8D10	Mouse
9C12	Mouse
6D12	Mouse

The DNA sequences encoding the complementarity determining regions (CDRs) for the rabbit monoclonal antibodies 20D4 and JA1 were determined and are provided in SEQ ID NO: 502 and 503, respectively.

In order to better define the epitope binding region of each of the antibodies, a series of overlapping peptides were generated that span amino acids 109-213 of SEQ ID NO: 114. These peptides were used to epitope map the anti-P503S monoclonal antibodies by ELISA as follows.

15 The recombinant fragment of P503S that was employed as the immunogen was used as a positive control. Ninety-six well microtiter plates were coated with either peptide or recombinant antigen at 20 ng/well overnight at 4 °C. Plates were aspirated and blocked with phosphate buffered saline containing 1% (w/v) BSA for 2 hours at room temperature then washed in PBS containing 0.1% Tween 20 (PBST). Purified rabbit monoclonal antibodies diluted in PBST were added to the wells

20 and incubated for 30 min at room temperature. This was followed by washing 6 times with PBST and incubation with Protein-A HRP conjugate at a 1:2000 dilution for a further 30 min. Plates were washed six times in PBST and incubated with tetramethylbenzidine (TMB) substrate for a further

15 min. The reaction was stopped by the addition of 1N sulfuric acid and plates were read at 450 nm using at ELISA plate reader. ELISA with the mouse monoclonal antibodies was performed with supernatants from tissue culture run neat in the assay.

All of the antibodies bound to the recombinant P503S fragment, with the exception of the negative control SP2 supernatant. 20D4, JA1 and 1D12 bound strictly to peptide #2101 (SEQ ID NO: 504), which corresponds to amino acids 151-169 of SEQ ID NO: 114. 1C3 bound to peptide #2102 (SEQ ID NO: 505), which corresponds to amino acids 165-184 of SEQ ID NO: 114. 9C12 bound to peptide #2099 (SEQ ID NO: 522), which corresponds to amino acids 120-139 of SEQ ID NO: 114. The other antibodies bind to regions that were not examined in these studies.

Subsequent to epitope mapping, the antibodies were tested by FACS analysis on a cell line that stably expressed P503S to confirm that the antibodies bind to cell surface epitopes. Cells stably transfected with a control plasmid were employed as a negative control. Cells were stained live with no fixative. 0.5 ug of anti-P503S monoclonal antibody was added and cells were incubated on ice for 30 min before being washed twice and incubated with a FITC-labelled goat anti-rabbit or mouse secondary antibody for 20 min. After being washed twice, cells were analyzed with an Excalibur fluorescent activated cell sorter. The monoclonal antibodies 1C3, 1D12, 9C12, 20D4 and JA1, but not 8D3, were found to bind to a cell surface epitope of P503S.

In order to determine which tissues express P503S, immunohistochemical analysis was performed, essentially as described above, on a panel of normal tissues (prostate, adrenal, breast, cervix, colon, duodenum, gall bladder, ileum, kidney, ovary, pancreas, parotid gland, skeletal muscle, spleen and testis). HRP-labeled anti-mouse or anti-rabbit antibody followed by incubation with TMB was used to visualize P503S immunoreactivity. P503S was found to be highly expressed in prostate tissue, with lower levels of expression being observed in cervix, colon, ileum and kidney, and no expression being observed in adrenal, breast, duodenum, gall bladder, ovary, pancreas, parotid gland, skeletal muscle, spleen and testis.

Western blot analysis was used to characterize anti-P503S monoclonal antibody specificity. SDS-PAGE was performed on recombinant (rec) P503S expressed in and purified from bacteria and on lysates from HEK293 cells transfected with full length P503S. Protein was transferred to nitrocellulose and then Western blotted with each of the anti-P503S monoclonal antibodies (20D4, JA1, 1D12, 6D12 and 9C12) at an antibody concentration of 1 ug/ml. Protein was detected using horse radish peroxidase (HRP) conjugated to either a goat anti-mouse monoclonal antibody or to protein A-sepharose. The monoclonal antibody 20D4 detected the

appropriate molecular weight 14 kDa recombinant P503S (amino acids 113-241) and the 23.5 kDa species in the HEK293 cell lysates transfected with full length P503S. Other anti-P503S monoclonal antibodies displayed similar specificity by Western blot.

5 **c) Preparation and Characterization of Antibodies against P703P**

Rabbits were immunized with either a truncated (P703Ptr1; SEQ ID NO: 172) or full-length mature form (P703Pfl; SEQ ID NO: 523) of recombinant P703P protein was expressed in and purified from bacteria as described above. Affinity purified polyclonal antibody was generated using immunogen P703Pfl or P703Ptr1 attached to a solid support. Rabbit monoclonal
10 antibodies were isolated using SLAM technology at Immgenics Pharmaceuticals. Table VII below lists both the polyclonal and monoclonal antibodies that were generated against P703P.

Table VII

Antibody	Immunogen	Species/type
Aff. Purif. P703P (truncated); #2594	P703Ptr1	Rabbit polyclonal
Aff. Purif. P703P (full length); #9245	P703Pfl	Rabbit polyclonal
2D4	P703Ptr1	Rabbit monoclonal
8H2	P703Ptr1	Rabbit monoclonal
7H8	P703Ptr1	Rabbit monoclonal

15

The DNA sequences encoding the complementarity determining regions (CDRs) for the rabbit monoclonal antibodies 8H2, 7H8 and 2D4 were determined and are provided in SEQ ID NO: 506-508, respectively.

Epitope mapping studies were performed as described above. Monoclonal
20 antibodies 2D4 and 7H8 were found to specifically bind to the peptides of SEQ ID NO: 509 (corresponding to amino acids 145-159 of SEQ ID NO: 172) and SEQ ID NO: 510 (corresponding to amino acids 11-25 of SEQ ID NO: 172), respectively. The polyclonal antibody 2594 was found to bind to the peptides of SEQ ID NO: 511-514, with the polyclonal antibody 9427 binding to the peptides of SEQ ID NO: 515-517.

25 The specificity of the anti-P703P antibodies was determined by Western blot analysis as follows. SDS-PAGE was performed on (1) bacterially expressed recombinant antigen; (2) lysates of HEK293 cells and Ltk-/- cells either untransfected or transfected with a plasmid

expressing full length P703P; and (3) supernatant isolated from these cell cultures. Protein was transferred to nitrocellulose and then Western blotted using the anti-P703P polyclonal antibody #2594 at an antibody concentration of 1 ug/ml. Protein was detected using horse radish peroxidase (HRP) conjugated to an anti-rabbit antibody. A 35 kDa immunoreactive band could be observed with recombinant P703P. Recombinant P703P runs at a slightly higher molecular weight since it is epitope tagged. In lysates and supernatants from cells transfected with full length P703P, a 30 kDa band corresponding to P703P was observed. To assure specificity, lysates from HEK293 cells stably transfected with a control plasmid were also tested and were negative for P703P expression. Other anti-P703P antibodies showed similar results.

Immunohistochemical studies were performed as described above, using anti-P703P monoclonal antibody. P703P was found to be expressed at high levels in normal prostate and prostate tumor tissue but was not detectable in all other tissues tested (breast tumor, lung tumor and normal kidney).

EXAMPLE 19

CHARACTERIZATION OF CELL SURFACE EXPRESSION AND CHROMOSOME LOCALIZATION OF THE PROSTATE-SPECIFIC ANTIGEN P501S

This example describes studies demonstrating that the prostate-specific antigen P501S is expressed on the surface of cells, together with studies to determine the probable chromosomal location of P501S.

The protein P501S (SEQ ID NO: 113) is predicted to have 11 transmembrane domains. Based on the discovery that the epitope recognized by the anti-P501S monoclonal antibody 10E3-G4-D3 (described above in Example 17) is intracellular, it was predicted that following transmembrane determinants would allow the prediction of extracellular domains of P501S. Fig. 9 is a schematic representation of the P501S protein showing the predicted location of the transmembrane domains and the intracellular epitope described in Example 17. Underlined sequence represents the predicted transmembrane domains, bold sequence represents the predicted extracellular domains, and italicized sequence represents the predicted intracellular domains. Sequence that is both bold and underlined represents sequence employed to generate polyclonal rabbit serum. The location of the transmembrane domains was predicted using HHMTOP as

described by Tusnady and Simon (Principles Governing Amino Acid Composition of Integral Membrane Proteins: Applications to Topology Prediction, *J. Mol. Biol.* 283:489-506, 1998).

Based on Fig. 9, the P501S domain flanked by the transmembrane domains corresponding to amino acids 274-295 and 323-342 is predicted to be extracellular. The peptide of SEQ ID NO: 518 corresponds to amino acids 306-320 of P501S and lies in the predicted extracellular domain. The peptide of SEQ ID NO: 519, which is identical to the peptide of SEQ ID NO: 518 with the exception of the substitution of the histidine with an asparagine, was synthesized as described above. A Cys-Gly was added to the C-terminus of the peptide to facilitate conjugation to the carrier protein. Cleavage of the peptide from the solid support was carried out using the following cleavage mixture: trifluoroacetic acid:ethanediol:thioanisole:water:phenol (40:1:2:2:3). After cleaving for two hours, the peptide was precipitated in cold ether. The peptide pellet was then dissolved in 10% v/v acetic acid and lyophilized prior to purification by C18 reverse phase hplc. A gradient of 5-60% acetonitrile (containing 0.05% TFA) in water (containing 0.05% TFA) was used to elute the peptide. The purity of the peptide was verified by hplc and mass spectrometry, and was determined to be >95%. The purified peptide was used to generate rabbit polyclonal antisera as described above.

Surface expression of P501S was examined by FACS analysis. Cells were stained with the polyclonal anti-P501S peptide serum at 10 µg/ml, washed, incubated with a secondary FITC-conjugated goat anti-rabbit Ig antibody (ICN), washed and analyzed for FITC fluorescence using an Excalibur fluorescence activated cell sorter. For FACS analysis of transduced cells, B-LCL were retrovirally transduced with P501S. To demonstrate specificity in these assays, B-LCL transduced with an irrelevant antigen (P703P) or nontransduced were stained in parallel. For FACS analysis of prostate tumor cell lines, Lncap, PC-3 and DU-145 were utilized. Prostate tumor cell lines were dissociated from tissue culture plates using cell dissociation medium and stained as above. All samples were treated with propidium iodide (PI) prior to FACS analysis, and data was obtained from PI-excluding (i.e. intact and non-permeabilized) cells. The rabbit polyclonal serum generated against the peptide of SEQ ID NO: 519 was shown to specifically recognize the surface of cells transduced to express P501S, demonstrating that the epitope recognized by the polyclonal serum is extracellular.

To determine biochemically if P501S is expressed on the cell surface, peripheral membranes from Lncap cells were isolated and subjected to Western blot analysis. Specifically, Lncap cells were lysed using a dounce homogenizer in 5 ml of homogenization buffer (250 mM

sucrose, 10 mM HEPES, 1mM EDTA, pH 8.0, 1 complete protease inhibitor tablet (Boehringer Mannheim)). Lysate samples were spun at 1000 g for 5 min at 4 °C. The supernatant was then spun at 8000g for 10 min at 4 °C. Supernatant from the 8000g spin was recovered and subjected to a 100,000g spin for 30 min at 4 °C to recover peripheral membrane. Samples were then separated by SDS-PAGE and Western blotted with the mouse monoclonal antibody 10E3-G4-D3 (described above in Example 17) using conditions described above. Recombinant purified P501S, as well as HEK293 cells transfected with and over-expressing P501S were included as positive controls for P501S detection. LCL cell lysate was included as a negative control. P501S could be detected in Lncap total cell lysate, the 8000g (internal membrane) fraction and also in the 100,000g (plasma membrane) fraction. These results indicate that P501S is expressed at, and localizes to, the peripheral membrane.

To demonstrate that the rabbit polyclonal antiserum generated to the peptide of SEQ ID NO: 519 specifically recognizes this peptide as well as the corresponding native peptide of SEQ ID NO: 518, ELISA analyses were performed. For these analyses, flat-bottomed 96 well microtiter plates were coated with either the peptide of SEQ ID NO: 519, the longer peptide of SEQ ID NO: 520 that spans the entire predicted extracellular domain, the peptide of SEQ ID NO: 521 which represents the epitope recognized by the P501S-specific antibody 10E3-G4-D3, or a P501S fragment (corresponding to amino acids 355-526 of SEQ ID NO: 113) that does not include the immunizing peptide sequence, at 1 µg/ml for 2 hours at 37 °C. Wells were aspirated, blocked with phosphate buffered saline containing 1% (w/v) BSA for 2 hours at room temperature and subsequently washed in PBS containing 0.1% Tween 20 (PBST). Purified anti-P501S polyclonal rabbit serum was added at 2 fold dilutions (1000 ng - 125 ng) in PBST and incubated for 30 min at room temperature. This was followed by washing 6 times with PBST and incubating with HRP-conjugated goat anti-rabbit IgG (H+L) Affinipure F(ab') fragment at 1:20000 for 30 min. Plates were then washed and incubated for 15 min in tetramethyl benzidine. Reactions were stopped by the addition of 1N sulfuric acid and plates were read at 450 nm using an ELISA plate reader. As shown in Fig. 11, the anti-P501S polyclonal rabbit serum specifically recognized the peptide of SEQ ID NO: 519 used in the immunization as well as the longer peptide of SEQ ID NO: 520, but did not recognize the irrelevant P501S-derived peptides and fragments.

In further studies, rabbits were immunized with peptides derived from the P501S sequence and predicted to be either extracellular or intracellular, as shown in Fig. 9. Polyclonal rabbit sera were isolated and polyclonal antibodies in the serum were purified, as described above.

To determine specific reactivity with P501S, FACS analysis was employed, utilizing either B-LCL transduced with P501S or the irrelevant antigen P703P, of B-LCL infected with vaccinia virus-expressing P501S. For surface expression, dead and non-intact cells were excluded from the analysis as described above. For intracellular staining, cells were fixed and permeabilized as described above. Rabbit polyclonal serum generated against the peptide of SEQ ID NO: 548, which corresponds to amino acids 181-198 of P501S, was found to recognize a surface epitope of P501S. Rabbit polyclonal serum generated against the peptide SEQ ID NO: 551, which corresponds to amino acids 543-553 of P501S, was found to recognize an epitope that was either potentially extracellular or intracellular since in different experiments intact or permeabilized cells were recognized by the polyclonal sera. Based on similar deductive reasoning, the sequences of SEQ ID NO: 541-547, 549 and 550, which correspond to amino acids 109-122, 539-553, 509-520, 37-54, 342-359, 295-323, 217-274, 143-160 and 75-88, respectively, of P501S, can be considered to be potential surface epitopes of P501S recognized by antibodies.

The chromosomal location of P501S was determined using the GeneBridge 4 Radiation Hybrid panel (Research Genetics). The PCR primers of SEQ ID NO: 528 and 529 were employed in PCR with DNA pools from the hybrid panel according to the manufacturer's directions. After 38 cycles of amplification, the reaction products were separated on a 1.2% agarose gel, and the results were analyzed through the Whitehead Institute/MIT Center for Genome Research web server (<http://www-genome.wi.mit.edu/cgi-bin/contig/rhmapper.pl>) to determine the probable chromosomal location. Using this approach, P501S was mapped to the long arm of chromosome 1 at WI-9641 between q32 and q42. This region of chromosome 1 has been linked to prostate cancer susceptibility in hereditary prostate cancer (Smith *et al. Science* 274:1371-1374, 1996 and Berthon *et al. Am. J. Hum. Genet.* 62:1416-1424, 1998). These results suggest that P501S may play a role in prostate cancer malignancy.

From the foregoing, it will be appreciated that, although specific embodiments of the invention have been described herein for the purposes of illustration, various modifications may be made without deviating from the spirit and scope of the invention. Accordingly, the present invention is not limited except as by the appended claims.

CLAIMS

1. An isolated polypeptide comprising at least an immunogenic portion of a prostate-specific protein, or a variant thereof, wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:

(a) sequences recited in any one of SEQ ID NO: 2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471, 472-476, 524, 526, 530, 531, 533, 535 and 536;

(b) sequences that hybridize to any of the foregoing sequences under moderately stringent conditions; and

(c) complements of any of the sequence of (a) or (b).

2. An isolated polypeptide according to claim 1, wherein the polypeptide comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID No: 2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471, 472-476, 524, 526, 530, 531, 533, 535 and 536, or a complement of any of the foregoing polynucleotide sequences.

3. An isolated polypeptide comprising a sequence recited in any one of SEQ ID NO: 108, 112, 113, 114, 172, 176, 178, 327, 329, 331, 339, 383, 477-483, 496, 504, 505, 519, 520, 522, 525, 527, 532, 534 and 537-550.

4. An isolated polynucleotide encoding at least 15 contiguous amino acid residues of a prostate-specific protein, or a variant thereof that differs in one or more substitutions, deletions, additions and/or insertions such that the ability of the variant to react with antigen-specific antisera is not substantially diminished, wherein the protein
5 comprises an amino acid sequence that is encoded by a polynucleotide comprising a sequence recited in any one of SEQ ID NO: 2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413,
10 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471, 472-476, 524, 526, 530, 531, 533, 535 and 536, or a complement of any of the foregoing sequences.

5. An isolated polynucleotide encoding a prostate-specific protein, or a
15 variant thereof, wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide comprising a sequence recited in any one of SEQ ID NO: 2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396,
20 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471, 472-476, 524, 526, 530, 531, 533, 535 and 536, or a complement of any of the foregoing sequences.

6. An isolated polynucleotide comprising a sequence recited in any one
25 of SEQ ID NO: 2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471, 472-476, 524, 526, 530,
30 531, 533, 535 and 536.

7. An isolated polynucleotide comprising a sequence that hybridizes under moderately stringent conditions to a sequence recited in any one of SEQ ID NO: 2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471, 472-476, 524, 526, 530, 531, 533, 535 and 536.

8. An isolated polynucleotide complementary to a polynucleotide according to any one of claims 4-7.

9. An expression vector comprising a polynucleotide according to any one of claims 4-8.

10. A host cell transformed or transfected with an expression vector according to claim 9.

11. An isolated antibody, or antigen-binding fragment thereof, that specifically binds to a prostate-specific protein, the protein comprising an amino acid sequence encoded by a polynucleotide sequence recited in any one of SEQ ID NO: 2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471, 472-476, 524, 526, 530, 531, 533, 535 and 536 or a complement of any of the foregoing polynucleotide sequences.

12. A monoclonal antibody that specifically binds to an amino acid sequence selected from the group consisting of SEQ ID NO: 496, 504, 505, 509-517, 519, 520, 522 and 539-551.

5 13. A monoclonal antibody comprising a complementarity determining region selected from the group consisting of SEQ ID NO: 502, 503 and 506-508.

10 14. A fusion protein comprising at least one polypeptide according to claim 1.

15 15. A fusion protein according to claim 14, wherein the fusion protein comprises an expression enhancer that increases expression of the fusion protein in a host cell transfected with a polynucleotide encoding the fusion protein.

16 16. A fusion protein according to claim 14, wherein the fusion protein comprises a T helper epitope that is not present within the polypeptide of claim 1.

20 17. A fusion protein according to claim 14, wherein the fusion protein comprises an affinity tag.

18. An isolated polynucleotide encoding a fusion protein according to claim 14.

25 19.. A pharmaceutical composition comprising a physiologically acceptable carrier and at least one component selected from the group consisting of:

- (a) a polypeptide according to claim 1;
- (b) a polynucleotide according to claim 4;
- (c) an antibody according to any one of claims 11-13;
- 30 (d) a fusion protein according to claim 14; and

(e) a polynucleotide according to claim 18.

20. A vaccine comprising an immunostimulant and at least one component selected from the group consisting of:

- 5 (a) a polypeptide according to claim 1;
(b) a polynucleotide according to claim 4;
(c) an antibody according to any one of claims 11-13;
(d) a fusion protein according to claim 14; and
(e) a polynucleotide according to claim 18.

10

21. A vaccine according to claim 20, wherein the immunostimulant is an adjuvant.

22. A vaccine according to claim 20, wherein the immunostimulant
15 induces a predominantly Type I response.

23. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a pharmaceutical composition according to claim 19.

20

24. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a vaccine according to claim 20.

25. A pharmaceutical composition comprising an antigen-presenting cell
25 that expresses a polypeptide according to claim 1, in combination with a pharmaceutically acceptable carrier or excipient.

26. A pharmaceutical composition according to claim 25, wherein the antigen presenting cell is a dendritic cell or a macrophage.

27. A vaccine comprising an antigen-presenting cell that expresses a polypeptide according to claim 1, in combination with an immunostimulant.

5 28. A vaccine according to claim 27, wherein the immunostimulant is an adjuvant.

29. A vaccine according to claim 27, wherein the immunostimulant induces a predominantly Type I response.

10

30. A vaccine according to claim 27, wherein the antigen-presenting cell is a dendritic cell.

31. A method for inhibiting the development of a cancer in a patient,
15 comprising administering to a patient an effective amount of an antigen-presenting cell that expresses a polypeptide encoded by a polynucleotide recited in any one of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535 and 536, and thereby inhibiting the development of a cancer in the patient.

20

32. A method according to claim 31, wherein the antigen-presenting cell is a dendritic cell.

33. A method according to any one of claims 23, 24 and 31, wherein the
25 cancer is prostate cancer.

34. A method for removing tumor cells from a biological sample, comprising contacting a biological sample with T cells that specifically react with a prostate-specific protein, wherein the protein comprises an amino acid sequence that is
30 encoded by a polynucleotide sequence selected from the group consisting of:

(i) polynucleotides recited in any one of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535 and 536; and

(ii) complements of the foregoing polynucleotides;

5 wherein the step of contacting is performed under conditions and for a time sufficient to permit the removal of cells expressing the prostate-specific protein from the sample.

35. A method according to claim 34, wherein the biological sample is
10 blood or a fraction thereof.

36. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient a biological sample treated according to the method of claim 50.

15

37. A method for stimulating and/or expanding T cells specific for a prostate-specific protein, comprising contacting T cells with at least one component selected from the group consisting of:

- (i) a polypeptide according to claim 1;
- 20 (ii) a polypeptide encoded by a polynucleotide comprising a sequence provided in any one of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535 and 536;
- (iii) a polynucleotide encoding a polypeptide of (i) or (ii); and
- (iv) an antigen presenting cell that expresses a polypeptide of (i) or (ii),
- 25 under conditions and for a time sufficient to permit the stimulation and/or expansion of T cells.

38. An isolated T cell population, comprising T cells prepared according to the method of claim 37.

30

39. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a T cell population according to claim 38.

5 40. A method for inhibiting the development of a cancer in a patient, comprising the steps of:

(a) incubating CD4⁺ and/or CD8⁺ T cells isolated from a patient with at least one component selected from the group consisting of:

(i) a polypeptide according to claim 1;
10 (ii) a polypeptide encoded by a polynucleotide comprising a sequence of any one of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535 and 536;

(iii) a polynucleotide encoding a polypeptide of (i) or (ii); or
15 (iv) an antigen-presenting cell that expresses a polypeptide of (i) or (ii);

such that T cells proliferate; and

(b) administering to the patient an effective amount of the proliferated T cells, and thereby inhibiting the development of a cancer in the patient.

20

41. A method for inhibiting the development of a cancer in a patient, comprising the steps of:

(a) incubating CD4⁺ and/or CD8⁺ T cells isolated from a patient with at least one component selected from the group consisting of:

(i) a polypeptide according to claim 1;
25 (ii) a polypeptide encoded by a polynucleotide comprising a sequence of any one of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535 and 536;

30 (iii) a polynucleotide encoding a polypeptide of (i) or (ii); or

(iv) an antigen-presenting cell that expresses a polypeptide of (i) or (ii);

such that T cells proliferate;

(b) cloning at least one proliferated cell to provide cloned T cells; and

5 (c) administering to the patient an effective amount of the cloned T cells, and thereby inhibiting the development of a cancer in the patient.

42. A method for determining the presence or absence of a cancer in a patient, comprising the steps of:

10 (a) contacting a biological sample obtained from a patient with a binding agent that binds to a prostate-specific protein, wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:

(i) polynucleotides recited in any one of SEQ ID NO: 1-111,
15 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535 and 536; and

(ii) complements of the foregoing polynucleotides;

(b) detecting in the sample an amount of polypeptide that binds to the binding agent; and

20 (c) comparing the amount of polypeptide to a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient.

43. A method according to claim 42, wherein the binding agent is an antibody.

25

44. A method according to claim 43, wherein the antibody is a monoclonal antibody.

45. A method according to claim 42, wherein the cancer is prostate
30 cancer.

46. A method for monitoring the progression of a cancer in a patient, comprising the steps of:

- 5 (a) contacting a biological sample obtained from a patient at a first point in time with a binding agent that binds to a prostate-specific protein, wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide sequence of any one of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535 and 536, or a complement of any of the foregoing polynucleotides;
- 10 (b) detecting in the sample an amount of polypeptide that binds to the binding agent;
- (c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and
- (d) comparing the amount of polypeptide detected in step (c) to the
15 amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.

47. A method according to claim 46, wherein the binding agent is an antibody.

20

48. A method according to claim 47, wherein the antibody is a monoclonal antibody.

49. A method according to claim 46, wherein the cancer is a prostate
25 cancer.

50. A method for determining the presence or absence of a cancer in a patient, comprising the steps of:

- 30 (a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes a prostate-specific protein,

wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide sequence of any one of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535 and 536, or a complement of any of the foregoing polynucleotides;

5 (b) detecting in the sample an amount of a polynucleotide that hybridizes to the oligonucleotide; and

(c) comparing the amount of polynucleotide that hybridizes to the oligonucleotide to a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient.

10

51. A method according to claim 50, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a polymerase chain reaction.

15

52. A method according to claim 50, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a hybridization assay.

53. A method for monitoring the progression of a cancer in a patient,
20 comprising the steps of:

(a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes a prostate-specific protein, wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide sequence of any one of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315,
25 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535 and 536, or a complement of any of the foregoing polynucleotides;

(b) detecting in the sample an amount of a polynucleotide that hybridizes to the oligonucleotide;

(c) repeating steps (a) and (b) using a biological sample obtained from
30 the patient at a subsequent point in time; and

(d) comparing the amount of polynucleotide detected in step (c) to the amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.

5 54. A method according to claim 53, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a polymerase chain reaction.

10 55. A method according to claim 53, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a hybridization assay.

 56. A diagnostic kit, comprising:
 (a) one or more antibodies according to claim 11; and
15 (b) a detection reagent comprising a reporter group.

 57. A kit according to claim 56, wherein the antibodies are immobilized on a solid support.

20 58. A kit according to claim 56, wherein the detection reagent comprises an anti-immunoglobulin, protein G, protein A or lectin.

 59. A kit according to claim 56, wherein the reporter group is selected from the group consisting of radioisotopes, fluorescent groups, luminescent groups,
25 enzymes, biotin and dye particles.

 60. An oligonucleotide comprising 10 to 40 contiguous nucleotides that hybridize under moderately stringent conditions to a polynucleotide that encodes a prostate-specific protein, wherein the protein comprises an amino acid sequence that is
30 encoded by a polynucleotide sequence recited in any one of SEQ ID NO: 2, 3, 8-29, 41-45,

47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 5 452, 453, 459-461, 468-476, 524, 526, 530, 531, 533, 535 and 536, or a complement of any of the foregoing polynucleotides.

61. A oligonucleotide according to claim 60, wherein the oligonucleotide comprises 10-40 contiguous nucleotides recited in any one of SEQ ID NO:
10 2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-476, 524, 526, 530, 531, 533, 535 and 536.

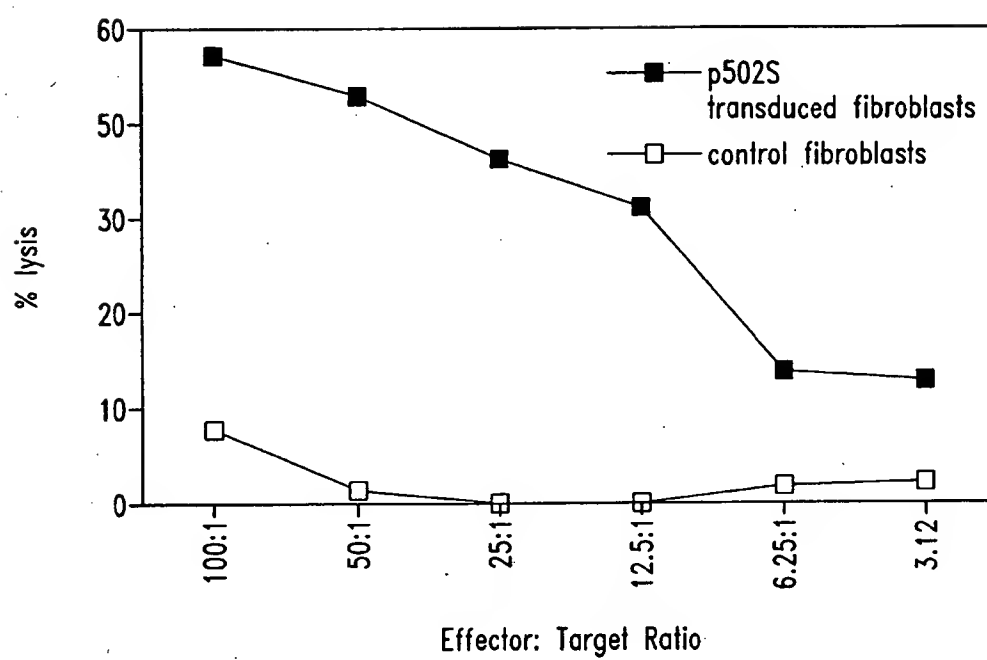
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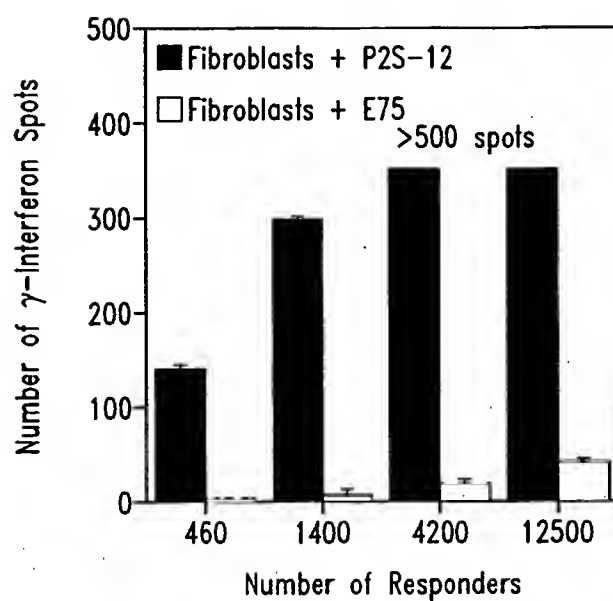
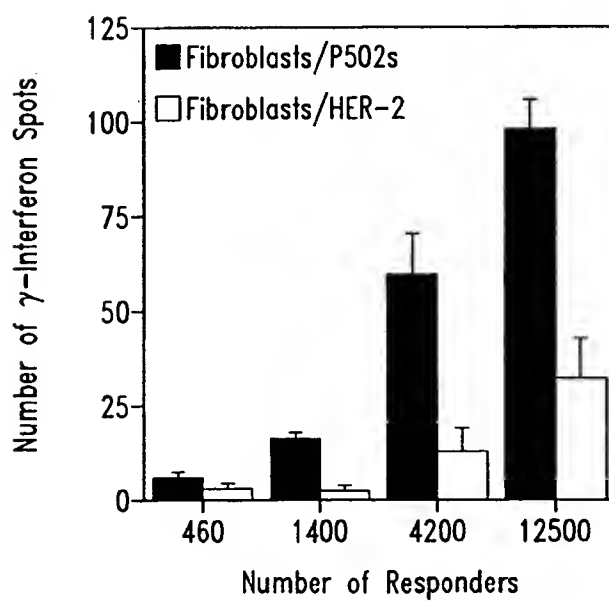
62. A diagnostic kit, comprising:
(a) an oligonucleotide according to claim 61; and
(b) a diagnostic reagent for use in a polymerase chain reaction or hybridization assay.

20

63. A host cell according to claim 10, wherein the cell is selected from the group consisting of: *E. coli*, baculovirus and mammalian cells.

64. A recombinant protein produced by a host cell according to claim
25 10.

*Fig. 1*

*Fig. 2A**Fig. 2B*

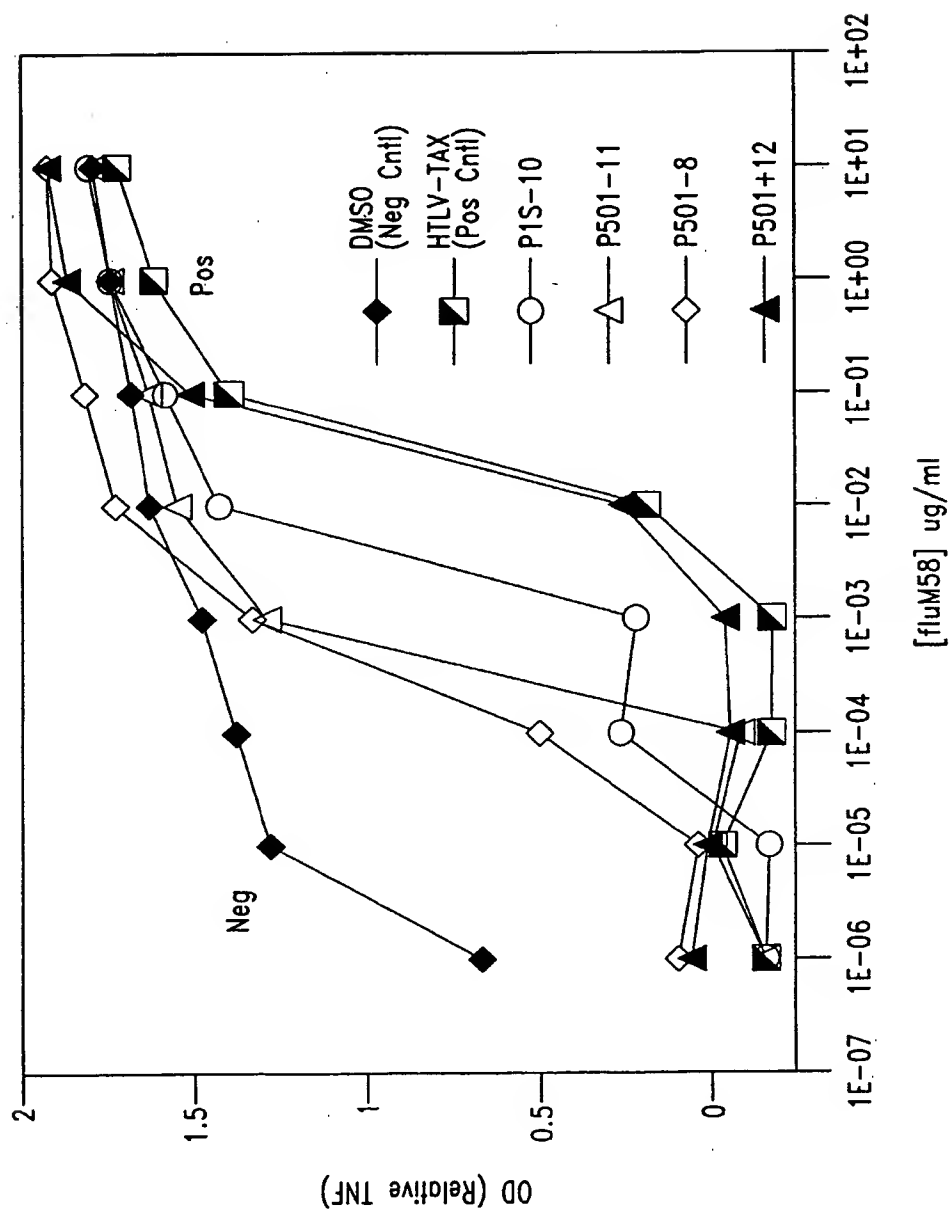
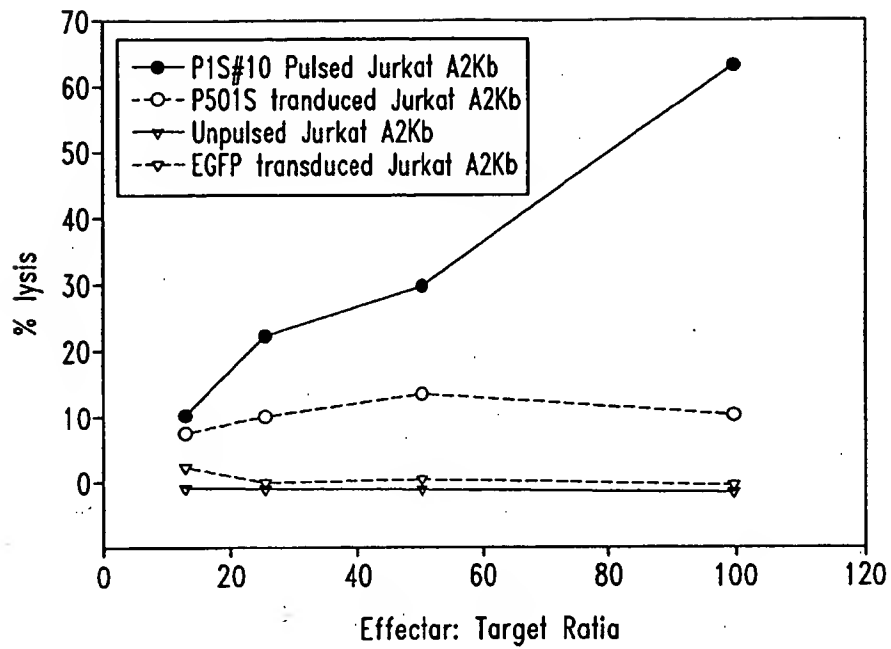
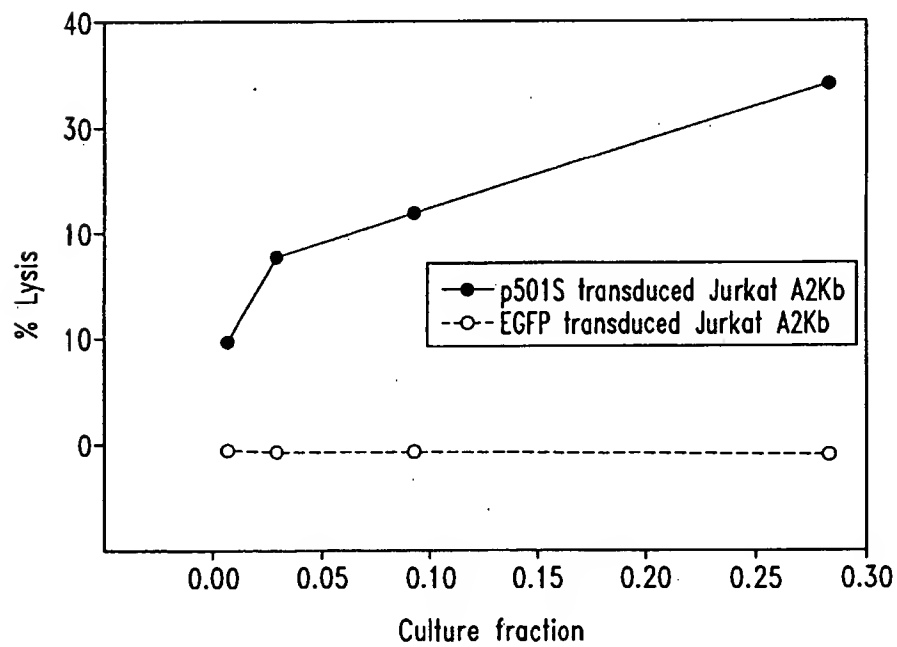
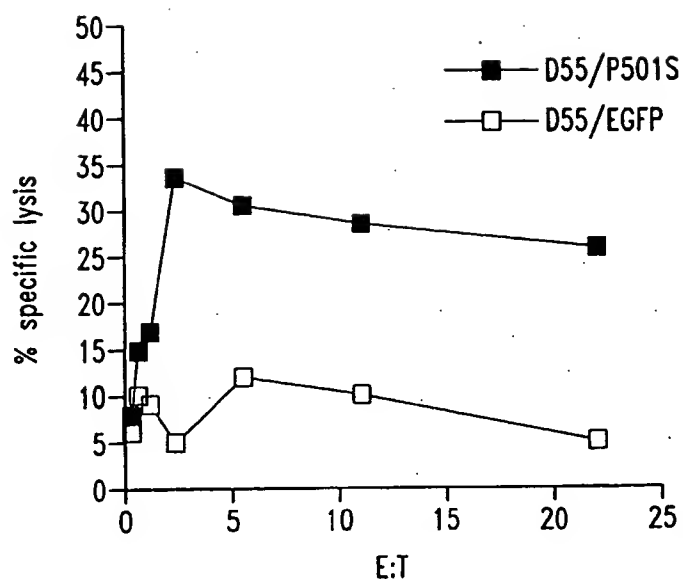
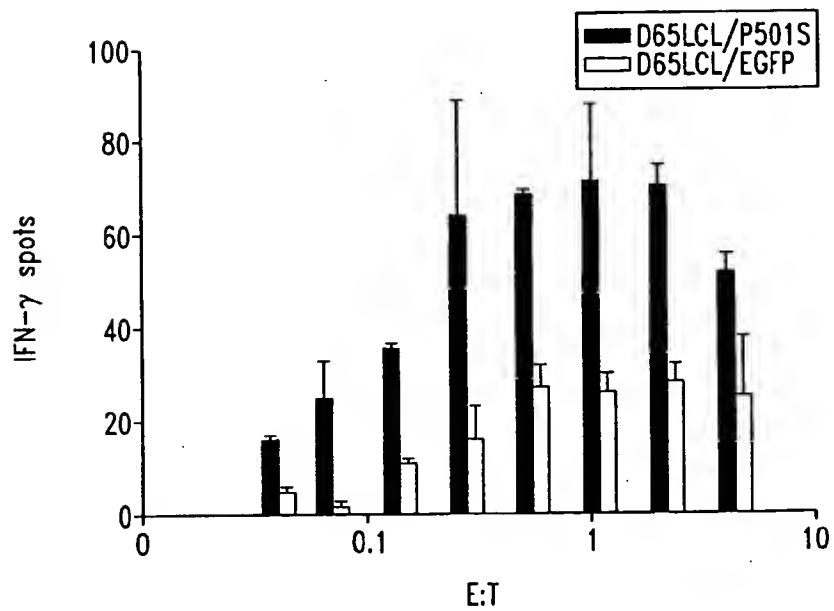
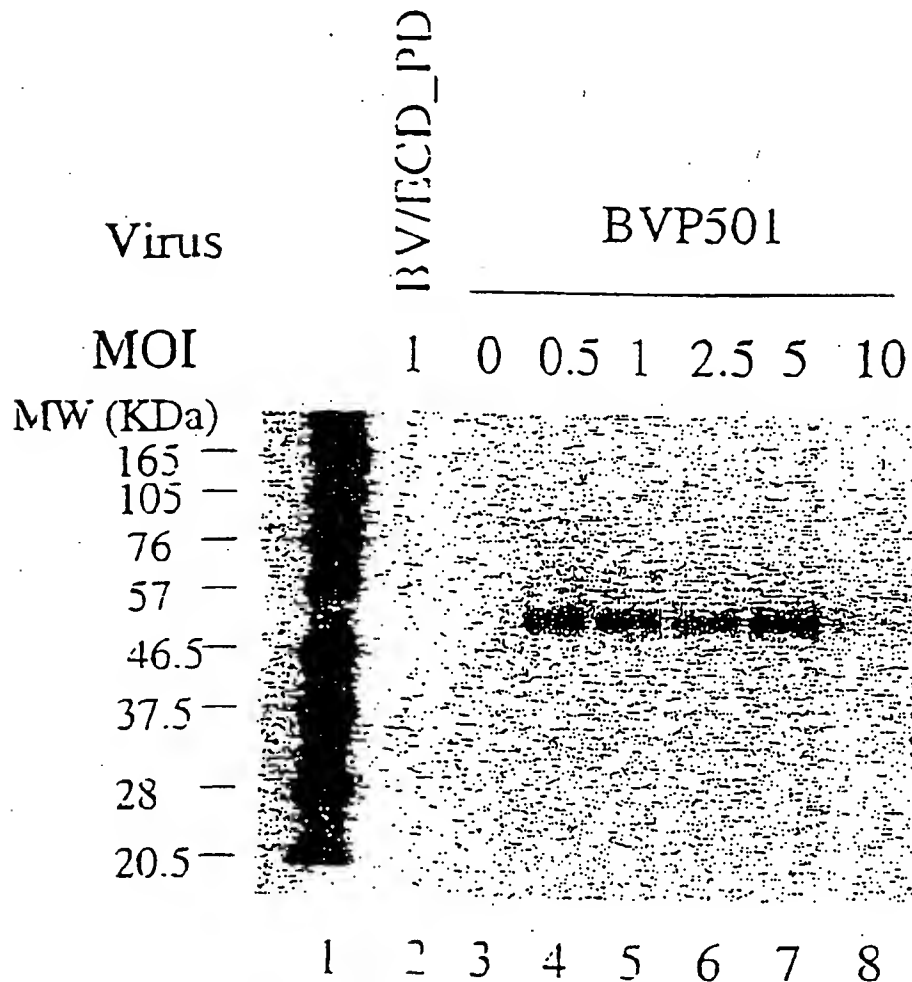


Fig. 3

*Fig. 4**Fig. 5*

*Fig. 6A**Fig. 6B*

Expression of P501S by the Baculovirus Expression System



0.6 million high 5 cells in 6-well plate were infected with an unrelated control virus BV/ECD_PD (lane 2), without virus (lane 3), or with recombinant baculovirus for P501 at different MOIs (lane 4 - 8). Cell lysates were run on SDS-PAGE under the reducing conditions and analyzed by Western blot with a monoclonal antibody against P501S (P501S-10E3-G4D3). Lane 1 is the biotinylated protein molecular weight marker (BioLabs).

Fig. 7

Figure 8. Mapping of the epitope recognized by 10E3-G4-D3

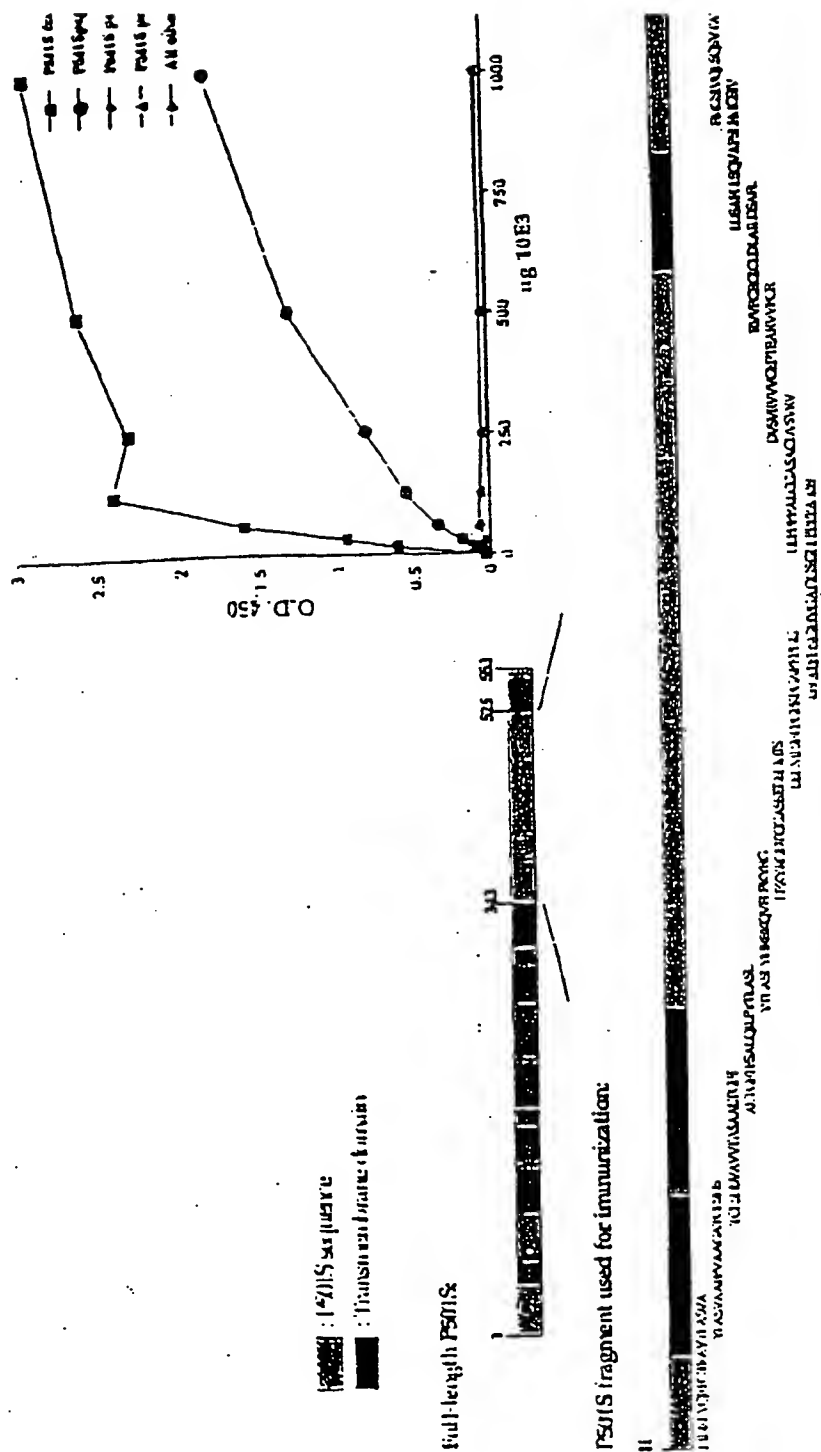


Fig. 8

Schematic of P501S with predicted
transmembrane, cytoplasmic, and extracellular regions

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 DHWRGRYGRRRP FIWALSLGILLSLFLIPRAGWL AGLLCPDPRPLE LALLILGVGLLDFCGQVCFTPL
EALLSDLFRDPDHCRQ AYSVYAFMISLGGCLGYLLPAI **DWDT**SALAPYLGTQEE
CLFGLLTLIFLTCVAATLLV AEEAALGPTEPAEGLSAPSLSPHCCPCRARLAFRNLGALLPRL
HQLCCRMPTLRR LFVAELCSWMALMTFTLFYTD VGEGLYQGVPR**AE**PGTEARRHYDEGVR
MGSLGLFLQCAISLVFSLVM DRLVQRFGTRAVYLAS VAAFPVAAGATCLSHSVAVVTA **SAA**
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LPPPPALCGASACDVSVRVVVGEPTEARVVPGRG ICLDLAILDSAFLLSQVAPSLF **MGSIVQLSQS**
VTAYMVSAAGLGLVAIYFAT **QVVF**DKSDLAKYSA

Underlined sequence: Predicted transmembrane domain; **Bold** sequence:
 Predicted extracellular domain; *Italic sequence*: Predicted intracellular
 domain. Sequence in bold/underlined: used generate polyclonal rabbit
 serum

Localization of domains predicted using HMMTOP (G.E. Tusnady and I. Simon
 (1998) Principles Governing Amino Acid Composition of Integral Membrane
 Proteins: Applications to topology Prediction. J. Mol Biol. 283, 489-506.

Fig. 9

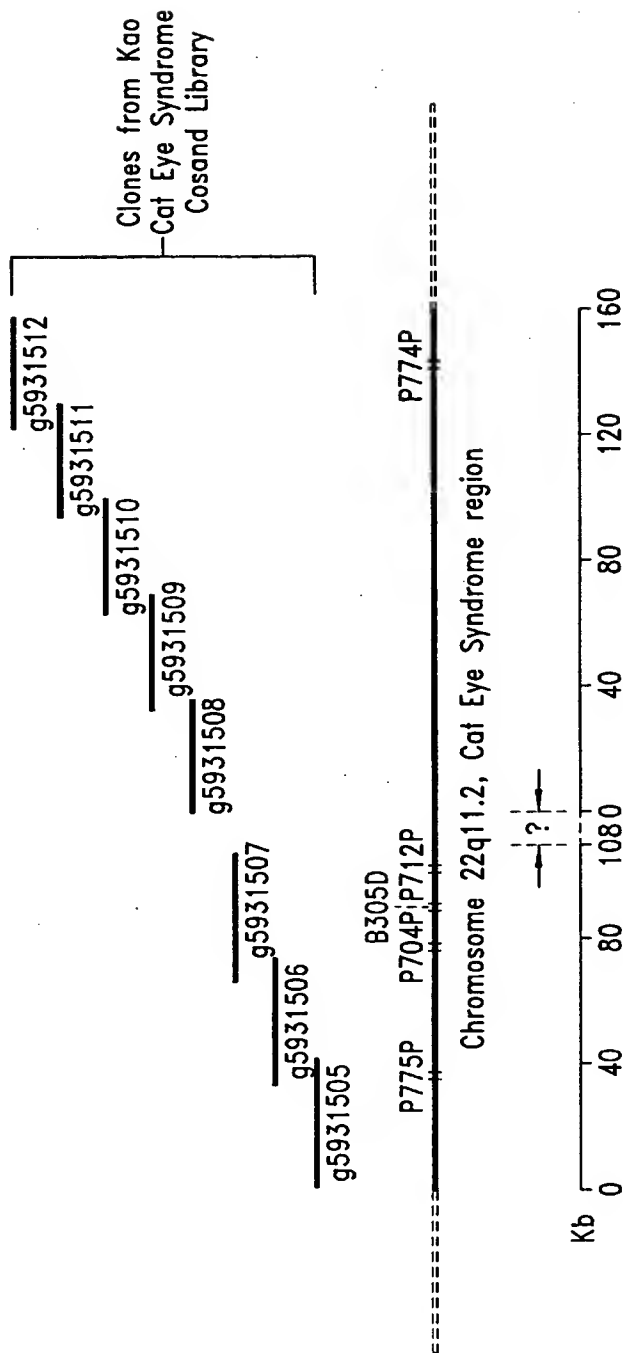
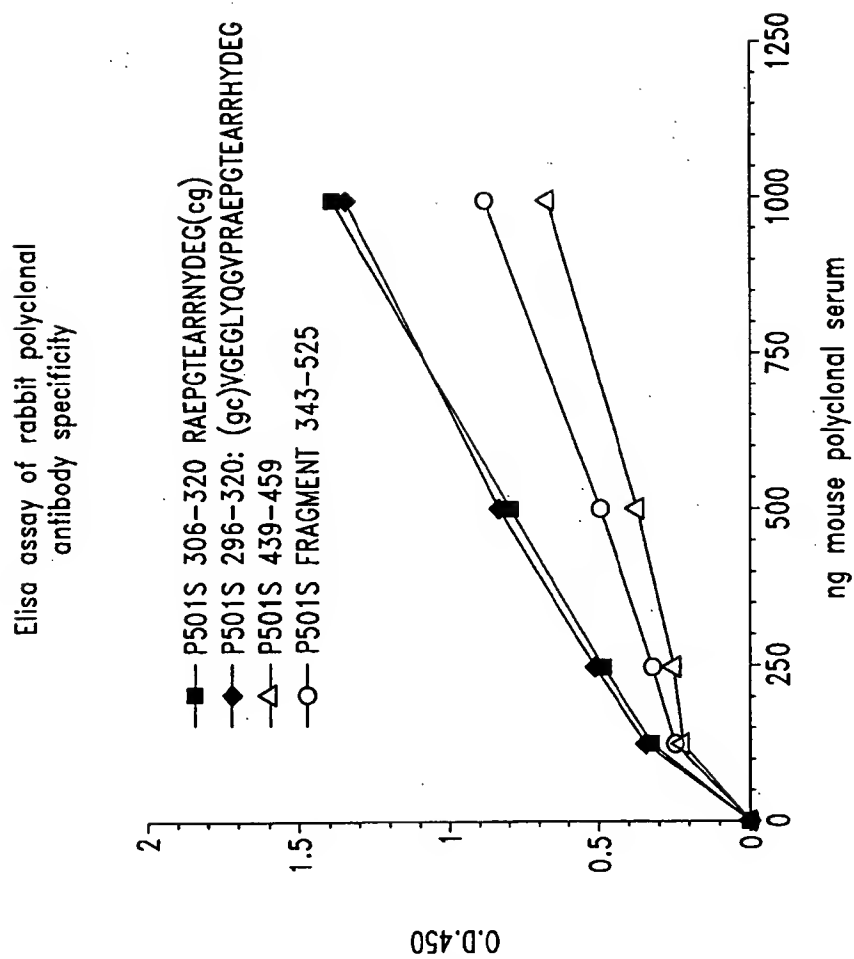


Fig. 10

*Fig. 11*

SEQUENCE LISTING

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 Harlocker, Susan Louise
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 Reed, Steven G.
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<213> Homo sapien

<220>

<221> misc_feature

<222> (1)... (801)

<223> n = A,T,C or G

<400> 9

acgccttgat	cctcccaggc	tgggactggt	tctgggagga	gccgggcatg	ctgtgggttg	60
taangatgac	actcccaaag	gtggtcctga	cagtggccca	gatggacatg	gggctcacct	120
caaggacaag	gccaccaggt	gcggggggcg	aagcccacat	gatccttact	ctatgagcaa	180
aatccccctgt	gggggcttct	ccttgaagtc	cgccancagg	gctcagtctt	tggaccang	240
caggtcatgg	ggttgtngnc	caactggggg	ccncaacgca	aaanggcnc	gggcctcngn	300
caccatccc	angacgcggc	tacactnctg	gacctccnc	tccaccactt	tcatgcgctg	360
ttcntaccg	cgnatntgtc	ccanctgttt	cngtgccnac	tccancttct	nggacgtgcg	420
ctacatacgc	ccggantcnc	netcccgtt	tgccctatc	cacgtncan	caacaaattt	480
cnccntantg	caccnattcc	cacntttnc	agntttcnc	nncngcttc	ctntaaaaag	540
ggttgancgc	cggaaaatnc	cccaaagggg	gggggcccng	tacccaactn	ccccctnata	600
gctgaantcc	ccatnaccnn	gnctcnatgg	ancntccnt	tttaannacn	ttctnaactt	660
gggaananc	ctcgnccntn	ccccnttaa	tccnccttg	cnangnnent	cccccnntcc	720
nccnnntng	gcntntnann	cnaaaaaggc	ccnnnancaa	tctcctnnen	cctcanttcg	780
ccanccctcg	aaatcgccn	c				801

<210> 10

<211> 789

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)... (789)

<223> n = A,T,C or G

<400> 10

cagtctatnt	ggccagtgtg	gcagctttcc	ctgtggctgc	cggtgccaca	tgctgtccc	60
acagtgtggc	cgtgggtgaca	gcttcagccg	ccctcacccg	gttcaccttc	tcagccctgc	120
agatcctgcc	ctacacactg	gcctccctct	accaccggga	gaagcaggtg	ttcctgccc	180
aataccgagg	ggacactgga	ggtgctagca	gtgaggacag	cctgatgacc	agcttccctg	240
caggccctaa	gcctggagct	ccctcccta	atggacacgt	gggtgctgga	ggcagtgggc	300
tgctcccacc	tccaccgcg	ctctgcgggg	cctctgcctg	tgatgtctcc	gtacgtgtgg	360
tgggtgggtga	gcccaccgan	gccaggggtg	ttccggggcg	gggcatctgc	ctggacctcg	420
ccatcctgga	tagtgcttcc	tgctgtccca	ngtggcccca	tccctgttta	tgggctccat	480
tgctcagctc	agccagctctg	tactgccta	tatgggtgtct	gccgcaggcc	tgggtctggt	540
cccatttact	ttgtacaca	ggtantattt	gacaagaacg	anttggccaa	atactcagcg	600
ttaaaaaatt	ccagcaacat	tgggggtgga	aggcctgcct	cactgggtcc	aactccccgc	660
tcctgttaac	cccatggggc	tgccggcttg	gccgccaat	tctgttgctg	ccaaantnat	720
gtggctctct	gctgccacct	gttgctggct	gaagtgcnta	cngcncanct	nggggggtng	780
gnggttccc						789

<210> 11

<211> 772

<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(772)
<223> n = A,T,C or G

<400> 11
 cccaccctac ccaaatatta gacaccaaca cagaaaagct agcaatggat tcccttctac 60
 tttgttaaat aaataagtta aatattttaa tgcctgtgtc tctgtgatgg caacagaagg 120
 accaacaggc cacatcctga taaaaggtaa gaggggggtg gatcagcaaa aagacagtgc 180
 tgtgggctga ggggacctgg ttcttgtgtg ttgcccctca ggactcttcc cctacaaata 240
 actttcatat gttcaaatcc catggaggag tgtttcatcc tagaaactcc catgcaagag 300
 ctacattaaa cgaagctgca ggtaagggg cttanagatg ggaaaccagg tgactgagtt 360
 tattcagctc ccaaaaaccc ttctctaggt gtgtctcaac taggaggcta gctgttaacc 420
 ctgagcctgg gtaatccacc tgcagatgcc ccgcattcca gtgcatggaa cccttctggc 480
 ctccctgtat aagtccagac tgaacccccc ttggaaggnc tccagtcagg cagccctana 540
 aactggggaa aaaagaaaaag gacgccccan cccccagctg tgcanctacg cacctcaaca 600
 gcaagggtg gcagcaaaaa aaccacttta ctttggcaca aacaaaaact ngggggggca 660
 accccggcac cccnangggg gttaacagga ancngggnaa cntggaaccc aattnaggca 720
 ggccnccac ccnaatntt gctgggaaat ttttctccc ctaaattntt tc 772

<210> 12
<211> 751
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(751)
<223> n = A,T,C or G

<400> 12
 gcccgaattc cagctgccac accaccacag gtgactgcat tagttcggat gtcatacaaa 60
 agctgattga agcaaccctc tacttttttg tctgagcct tttgcttggg gcaggtttca 120
 ttggctgtgt tggtagcgtt gtcattgcaa cagaatgggg gaaaggcact gttctctttg 180
 aagtanggtg agtccctcaa atccgtatag ttggtgaagc cacagcactt gagcccttcc 240
 atggtggtgt tccacacttg agtgaagtct tcctgggaac cataatcttt cttgatggca 300
 ggcactacca gcaacgtcag ggaagtgtc agccattgtg gtgtacacca aggcgaccac 360
 agcagctgcn acctcagcaa tgaagatgan gaggangatg aagaagaacg tcncgagggc 420
 acacttgctc tcagtcttan caccatanca gcccntgaaa accaananca aagaccacna 480
 cnccggctgc gatgaagaaa tnacccncg ttgacaaact tgcatggcac tggganccac 540
 agtggcccna aaaatcttca aaaaggatgc cccatcnatt gaccccccaa atgccactg 600
 ccaacagggg ctgccccacn cncnnaacga tgancnatt gnacaagatc tncntggtct 660
 tnatnaacnt gaaccctgcn tngtggctcc tggtcaggnc cnggcctga cttctnaann 720
 aangaactcn gaagncacca cngganannc g 751

<210> 13
<211> 729
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(729)
<223> n = A,T,C or G

<400> 13

gagccaggcg	tccctctgcc	tgcccaactca	gtggcaacac	ccgggagctg	ttttgtcctt	60
tgtggancct	cagcagtncc	ctctttcaga	actcantgcc	aaganccctg	aacaggagcc	120
accatgcagt	gcttcagctt	cattaagacc	atgatgatec	tcttcaattt	gctcatcttt	180
ctgtgtggtg	cagccctggt	ggcagtgggc	atctgggtgt	caatcgatgg	ggcatccttt	240
ctgaagatct	tggggccact	gtcgtccagt	gccatgcagt	ttgtcaacgt	gggctacttc	300
ctcatcgcat	ccggcggtgt	ggtcttagct	ctagggtttcc	tgggctgcta	tgggtgctaag	360
actgagagca	agtgtgccct	cgtgaogttc	ttcttcatcc	tcctcctcat	cttcattgct	420
gagggttgc	tgctgtggtc	gccttggtgt	acaccacaat	ggctgagcac	ttcctgacgt	480
tgctggtaat	gcctgccatc	aanaaaagat	tatgggttcc	caggaanact	tcactcaagt	540
gttggaacac	caccatgaaa	gggctcaagt	gctgtggctt	cnncacaacta	taaggatttt	600
gaagantcac	ctacttcaaa	gaaaanagtg	cctttccccc	atttctgttg	caattgacaa	660
acgtcccaaa	cacagccaat	tgaaaacctg	cacccaaccc	aaanggggtcc	ccaaccanaa	720
attnaagg						729

<210> 14

<211> 816

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (816)

<223> n = A,T,C or G

<400> 14

tgctcttct	caaagttggt	cttgttgcca	taacaaccac	cataggtaaa	gcgggcgcag	60
tgctcgctga	aggggttgta	gtaccagcgc	gggatgctct	ccttgccagag	tcctgtgtct	120
ggcagggtcca	cgagtgccc	ttgtcactg	gggaaatgga	tgcgctggag	ctcgtcaaag	180
ccactcgtgt	atttttcaca	ggcagcctcg	tccgacgcgt	cggggcagtt	gggggtgtct	240
tcacactcca	ggaaactgtc	natgcagcag	ccattgctgc	agcggaaactg	ggtgggtgta	300
cangtgccag	agcacactgg	atggcgctt	tccatggnan	gggcccctgng	ggaaagtccc	360
tganccecan	anctgectct	caaangeccc	acettgcaca	ccccgcacagg	ctagaatgga	420
atcttcttcc	cgaaaggtag	ttnttcttgt	tgcccaancc	anccccntaa	acaaactctt	480
gcanatctgc	tccgnggggg	tcntantacc	ancgtgggaa	aagaacccca	ggcngcgaa	540
caancttggt	tggatnccga	gcnaatatct	ncntttctgc	ttggtggaca	gcaccantna	600
ctgtnnanct	ttagnccttg	gtcctcntgg	ggtgnncttg	aacctaaten	ccnntcaact	660
gggacaaggt	aantngccnt	cctttnaatt	ccnancntn	ccccctgggt	tggggttttn	720
cnctctcta	cccagaaan	ncgtgttcc	cccccaacta	ggggccnaaa	ccnnttnttc	780
cacaacctn	ccccacccac	gggttcngnt	ggttng			816

<210> 15

<211> 783

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (783)

<223> n = A,T,C or G

<400> 15

ccaaggcctg	ggcaggcata	nacttgaagg	tacaacccca	ggaacccctg	gtgctgaagg	60
atgtggaaaa	cacagattgg	cgctactgc	gggttgacac	ggatgtcagg	gtagagagga	120
aagacccaaa	ccaggtggaa	ctgtggggac	tcaaggaang	cacctacctg	ttccagctga	180
cagtgactag	ctcagaccac	ccagaggaca	cggccaacgt	cacagtcact	gtgctgtcca	240
ccaagcagac	agaagactac	tgctcgcct	ccaacaangt	gggtcgctgc	cggggctctt	300
tccaacgctg	gtactatgac	cccacggagc	agatctgcaa	gagtttctgt	tatggagggt	360

gcttgggcaa	caagaacaac	taccttcggg	aagaagagt	cattctancc	tgtcnggggtg	420
tgcaagggtg	gcctttgana	ngcanctctg	gggctcangc	gactttcccc	cagggcccct	480
ccatggaaa	gcgccatcca	ntgttctctg	gcacctgtca	gcccacccag	ttccgctgca	540
ncaatggctg	ctgcatcnac	antttcctng	aattgtgaca	acacccccca	ntgcccccaa	600
ccctcccaac	aaagcttccc	tgttnaaaaa	tacnccantt	ggcttttnac	aaacncccg	660
cncctcctt	ttccccnntn	aacaaagggc	nctngcnttt	gaactgcecn	aaccnnggaa	720
tctnccnngg	aaaaantncc	ccccctgggt	cctnnaance	cctccncaaa	anctncccc	780
ccc						783

<210> 16

<211> 801

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(801)

<223> n = A,T,C or G

<400> 16

gccccaatc	cagctgccac	accacccacg	gtgactgcat	tagttcggat	gtcatacaaa	60
agctgattga	agcaaccctc	tacttttttg	tcgtgagcct	tttgcttgg	gcaggtttca	120
ttggctgtgt	tggtgacgtt	gtcattgcaa	cagaatgggg	gaaaggcact	gttctctttg	180
aagtagggtg	agtccctcaaa	atccgtatag	ttggtgaagc	cacagcactt	gagccctttc	240
atggtgggtg	tcacacactt	agtgaagtct	tcctgggaac	cataatcttt	cttgatggca	300
ggcactacca	gcaacgtcag	gaagtgtctc	gccattgtgg	tgtacaccaa	ggcgaccaca	360
gcagctgcaa	cctcagcaat	gaagatgagg	aggaggatga	agaagaacgt	cncgagggca	420
cacttgctct	ccgtcttagc	accatagcag	cccangaaac	caagagcaaa	gaccacaacg	480
ccngctgcga	atgaaagaaa	ntacccacgt	tgacaaaact	catggccact	ggacgcacgt	540
tgccccgaan	atcttcagaa	aagggatgcc	ccatcgattg	aacacccana	tgccactgc	600
cnacagggtg	gcncncncn	gaaagaatga	gccattgaag	aaggatcttc	ntggtcttaa	660
tgaactgaaa	ctntgcatgg	tggccctgtg	tcagggtctc	tggcagtgaa	ttctganaaa	720
aaggaaacng	ntnagcccc	ccaaangana	aaacaccccc	gggtgttgcc	ctgaattggc	780
ggccaaggan	ccctgccccn	g				801

<210> 17

<211> 740

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(740)

<223> n = A,T,C or G

<400> 17

gtgagagcca	ggcgtccctc	tgcctgccca	ctcagtggca	acacccggga	gctgttttgt	60
cctttgtgga	gcctcagcag	ttccctcttt	cagaactcac	tgccaagagc	cctgaacagg	120
agccaccatg	cagtgtctca	gcttcattaa	gaccatgatg	atcctcttca	atttgctcat	180
ctttctgtgt	ggtgcagccc	tgttggcagt	gggcatctgg	gtgtcaatcg	atggggcctc	240
ctttctgaag	atcttcgggc	cactgtcgtc	cagtggcatg	cagtttgtca	acgtgggcta	300
cttctctcat	gcagccggcg	ttgtggtctt	tgctcttggg	ttcctgggct	gctatgggtg	360
taagacggag	agcaagtgtg	ccctcgtgac	gttcttcttc	atcctcctcc	tcctcttcat	420
tgtgaagtt	gcagctgctg	tggtgcctt	ggtgtacacc	acaatggctg	aaccattcct	480
gacgttgctg	gtantgcctg	ccatcaanaa	agattatggg	ttcccaggaa	aaattcactc	540
aantntggaa	caccnccatg	aaaagggtc	caatttctgn	tggcttcccc	aactataccg	600
gaattttgaa	agantcnc	tacttccaaa	aaaaaanant	tgcttttnc	ccntttctgt	660
tgcaatgaaa	acntcccaan	acngccaatn	aaaacctgcc	cnnncaaaaa	ggntcncaaa	720

caaaaaaant nnaagggtn

740

<210> 18
 <211> 802
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(802)
 <223> n = A,T,C or G

<400> 18
 ccgctgggttg cgctgggtcca gngnagccac gaagcacgtc agcatacaca gcctcaatca 60
 caaggtcttc cagctgccc acattacgca gggcaagagc ctccagcaac actgcatatg 120
 ggatacactt tactttagca gccagggtga caactgagag gtgtcgaagc ttattcttct 180
 gagcctctgt tagtggagga agattccggg cttcagctaa gtatgcagcg tatgtcccat 240
 aagcaaacac tgtgagcagc cggaaggtag aggcaaagtc actctcagcc agctctctaa 300
 cattgggcat gtccagcagt tctccaaaca cgtagacacc agnggcctcc agcacctgat 360
 ggatgagtgt ggccagcgtt gccccccttg cgcacttggc taggagcaga aattgtctct 420
 ggttctgccc tgtcaccttc acttccgcac tcatcactgc actgagtgtg ggggacttgg 480
 gctcaggatg tccagagacg tggttccgcc cctcncctta atgacaccgn ccanncaacc 540
 gtcggctccc gccgantgng ttcgtcgtnc ctgggtcagg gtctgctggc cncacttgc 600
 aancctcgtc nggcccatgg aattcacnc accggaactn gtangatcca ctnnttctat 660
 aaccggncgc caccgcnntt ggaactccac tctnttnc tttacttgag ggtaaggtc 720
 acccttnncg ttaccttgg ccaaaccntn cctgtgtgcg anatngtnaa tcnggncna 780
 tnccancnc atangaagcc ng 802

<210> 19
 <211> 731
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(731)
 <223> n = A,T,C or G

<400> 19
 cnaagcttcc aggtnacggg ccgnaancc tgaccnagg tancanaang cagnncgagg 60
 gagcccaccg tcacgnggng gngtctttat nggagggggc ggagccacat cnetggacnt 120
 cntgacccca actcccnc ncncantgca gtgatgagtg cagaactgaa ggtnacgtgg 180
 caggaaacca gancaaannc tgctccnntc caagtcggcn nagggggcgg ggctggccac 240
 gencatecnt cnagtgtgtn aaagcccnn cctgtctact tgtttgaga acngcnnga 300
 catgcccagn gttanataac nggcngagag tnantttgcc tctcccttcc ggetgcgcan 360
 cgngtntgct tagnggacat aacctgacta cttaactgaa cccnngaate tncnccccct 420
 ccactaagct cagaacaaaa aacttcgaca ccactcantt gtcacctgnc tgctcaagta 480
 aagtgtaccc catnccaat gtntgctnga ngetctgncc tgcnttangt tcggctctgg 540
 gaagacctat caattnaagc tatgtttctg actgcctctt gctccctgna acaancnacc 600
 cnncnntcca agggggggnc ggcccccaat ccccccaacc ntnaattnan ttanccccn 660
 ccccnnggcc cggcctttta cnancntcnn nnacngggna aaacnnngc ttncccaac 720
 nnaatcnc t 731

<210> 20
 <211> 754
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(754)
 <223> n = A,T,C or G

<400> 20
 . tttttttttt tttttttttt taaaaacccc ctccattnaa tgnaaacttc cgaaattgtc 60
 caaccccctc ntccaaatnn ccntttccgg gnggggggttc caaacccaan ttanntttgg 120
 annttaaatt aaatnttntt tggnggnnna anccnaatgt nangaaagtt naaccanta 180
 tnancttnaa tncctggaaa ccngtngntt ccaaaaatnt ttaaccctta antccctccg 240
 aaatngttna nggaaaaccc aanttctcnt aaggttgttt gaaggntnaa tnaaaanccc 300
 nnccaattgt ttttngccac gcctgaatta attggnttcc gntgttttcc nttaaaanaa 360
 ggnnancccc ggttantnaa tcccccnnc cccaattata ccganttttt ttngaattgg 420
 gancccnccg gaattaacgg ggnnnntccc tnttgggggg cnggnncccc cccntcggg 480
 ggttngggnc aggnccnaat tgtttaaggg tccgaaaaat ccctccnaga aaaaaanctc 540
 ccaggttgag nntnggggtt ncccccccc cangggccct ctcgnanagt tggggtttgg 600
 ggggcctggg atttntttt cccnttntcc tcccccccc ccnggganag aggttngngt 660
 tttgntcnnn ggccccnccn aaganctttn ccganttnan ttaaatccnt gcctnggcga 720
 agtcctttgn agggntaaan ggccccctnn cggg 754

<210> 21
 <211> 755
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(755)
 <223> n = A,T,C or G

<400> 21
 atcancccat gacccnaac nngggaccnc tcanccggnc nnncnaccnc cggccnatca 60
 nngtnagnnc actncnnttn natcacnccc cncnactac gcccnananc cnacgcncta 120
 nncanatncc actganngcg cgangtngan ngagaaanct nataccanag ncaccanacn 180
 ccagctgtcc nanaangcct nnnatacnng nnnatccaat ntgnancctc cnaagtattn 240
 nncnncanat gattttcctn anccgattac ccntncccc tanccctcc cccccaacna 300
 cgaaggcnct ggncnaagg nngcgnccnc ccgctagntc cccncaagt cncnnccta 360
 aactcancn nattacnccg ttcttgagta tcaactcccc aatctcaccc tactcaactc 420
 aaaaanatch gatacaaaat aatncaagcc tgnttatnac actntgactg ggtctctatt 480
 ttagnygtcc ntnaanctc ctaatacttc cagctcncct tcnccaattt ccnaangget 540
 ctttcngaca gcatnttttg gttcccnntt gggttcttan ngaattgccc ttctnngaac 600
 gggctcntct tttccttcgg ttanccctgg ttcnncgggc cagttattat ttcccntttt 660
 aaattcntnc cntttanttt tggcnttca aacccccggc cttgaaaacg gccccctggg 720
 aaaaggttgt tttganaaaa tttttgtttt gttcc 755

<210> 22
 <211> 849
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(849)
 <223> n = A,T,C or G

<400> 22
 tttttttttt tttttangtg tngtcgtgca ggtagaggct tactacaant gtgaanacgt 60
 acgctnngan taangcgacc cgantttctag gannncnccct aaaatcanac tgtgaagatn 120

atcctgnnna	cggaanggtc	accggnngat	nntgctaggg	tgncenctcc	cannncttn	180
cataactcng	nggccctgcc	caccaccttc	ggcgcccnng	ngncegggcc	cgggtcattn	240
gnnttaaccn	cactnngcna	ncggtttccn	nccccnncng	accnnggcga	tccgggggtnc	300
tctgtcttcc	cctgnagncn	anaaantggg	ccncgggnccc	ctttaccct	nnacaagcca	360
cngccttcta	ncncngccc	cccctccant	nngggggact	gccnanngt	ccgttntctng	420
nnaccccnnn	gggtncctcg	gttgtegant	cnaccgnang	ccanggattc	cnaaggaagg	480
tgcgttnttg	gccccctacc	ttcgctnecg	nnaccccttc	ccgacnanga	nccgctcccg	540
cncnncgnng	cctcncctcg	caacacccgc	nctentcngt	ncggnnnccc	ccccaccgc	600
nccctcnenc	ngncgnannc	ctccnccncc	gtctcannca	ccaccccgcc	ccgccaggcc	660
ntcanccacn	ggngacnng	nagcncnntc	gcncgcgcgn	gcgnccct	cgcncngaa	720
ctnctcngg	ccantnnccg	tcaanccnna	cnaaacgcg	ctgcgcggcc	cgnagcgncc	780
ncctccncca	gtcctcccg	cttcnacc	angnttccn	cgaggacacn	nnaccccgcc	840
nncangcgg						849

<210> 23
 <211> 872
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(872)
 <223> n = A,T,C or G

<400> 23	
gcgcaaacta	tacttcgctc
tctgacnanc	ccgattnggc
cacacnncan	aganaaatcc
nggcgaatcg	taatnaggcg
ctnccnacc	tactctctcn
tggggttttn	nntgaccgng
nanngcncgc	nccccgnnet
accgcattga	ccctcgccnn
tgggnnngcg	tctgncgcgc
ccncgccttc	tcnnncaenc
cgnctgncgc	cgnccccacc
cnancngncn	gtcanccnag
cgaanantcc	tcnccntcan
ntctcccccg	ngngcncntc
tnaccnntac	gantnttcgn
gnactcgctc	gcctcgctnc
ngatctcnan	aagntcganc
nctgccttcc	anagtanacn
tgcgccgcca	atntgtcncc
nagctgtcnn	acccctngtn
cnnccccctcc	ccccntccat
cttcgcncnc	ctgtccctntn
ctnccnngaaa	ncgnanacgt
gttccttccn	ncncttcca
cctgggaecgc	tntcctntgc
ntcatttnca	nacgntcttc
ggaaggnggg	ggnnccnntg
cncctacctc	cgggcgnnet
tcagcctcnc	cccccncnt
cncctctttt	cc
cgcaaccatg	60
gantaacaca	120
agaaccangc	180
ccagctcnc	240
naggtcgggga	300
ccgcaccacc	360
ctggcncngn	420
annancgctg	480
tacnggggtct	540
tccccccctt	600
ggntnnctcc	660
nggngangtc	720
aacttancaa	780
tntctgtctc	840
	872

<210> 24
 <211> 815
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(815)
 <223> n = A,T,C or G

<400> 24	
gcatgcaagc	ttgagtattc
nctgncttcc	tgtgtcaa
tctnccattc	gtatacnaa
cgcattnccn	gencantatn
gncctctgac	tggnagagat
aanaccccc	cgcnngccac
tatagngtca	cctaaatanc
tanatatgaa	tctnatntga
canattecca	tnnattnccn
ncacnncat	ctatctncc
nacatgttca	tcttgatttn
ccaagacctc	ctgtggagggt
catggtenta	60
caaganngtc	120
tnnattnccn	180
ctatctncc	240
tcttgatttn	300
ctgtggagggt	360


```

aacctgcgtc aganncatca aacntgggaa acccgcnccc angtnnaagt ngnnncanan 420
gateccgtcc aggnntnacc atcccttcnc agcgccccct ttngtgcctt anagnnagc 480
gtgtccnanc cnetcaacat ganacgcgcc agnccanccg caattnggca caatgtcgnc 540
gaacccccta gggggantna tncaaanccc caggattgtc cncncangaa atcccnanc 600
ccnccctac ccncttttg gacngtgacc aantcccga gtncagtc gcccnctc 660
ccccaccggt nncntgggg ggggtgaanct cngnntcanc cngncgagg ntcgnaagga 720
accggnccctn ggncgaanng ancnntcnga agngccnct cgtataaccc cccctcncca 780
nccnacngnt agntcccccc cngggtnccg aangg 815

```

<210> 25

<211> 775

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(775)

<223> n = A,T,C or G

<400> 25

```

ccgagatgtc tgcctccgtg gccttagctg tgctcgcgt actctctctt tctggcctgg 60
aggctatcca gcgtactcca aagattcagg ttactcacg tcatccagca gagaatggaa 120
agtcaaattt cctgaattgc tatgtgtctg ggtttcatcc atccgacatt gaanttgact 180
tactgaagaa tgganagaga attgaaaaag tggagcatte agacttgtct ttcagcaagg 240
actggtcttt ctatctcntg tactacactg aattcacccc cactgaaaaa gatgagtatg 300
cctgccgtgt gaaccatgtg actttgtcac agcccaagat agttaagtgg gatcgagaca 360
tgtaagcagn cncatggaa gtttgaagat gccgcatttg gattggatga attccaaatt 420
ctgcttgctt gcnttttaat antgatatgc ntataacccc taccctttat gnceccaaat 480
tgtaggggtt acatnantgt tcnctnngga catgatcttc ctttataant cncncttcg 540
aattgccctt cncnctnngt ngaatgtttc cnaaccaag gttggctccc ccaggtcncc 600
tcttagcgaa gggcctgggc cnccttncaa ggttggggga accnaaaatt tcnctntgc 660
cncnccca cnccttngg mncnctttt ggaacccttc cnattccct tggcctcnaa 720
nccttnncta anaaaacttn aaancgtngc naaanntttt acttcccccc ttacc 775

```

<210> 26

<211> 820

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(820)

<223> n = A,T,C or G

<400> 26

```

anattantac agtgtaatct tttcccagag gtgtgtanag ggaacggggc ctagaggcat 60
cccanagata ncttatanca acagtgtttt gaccaagagc tgctgggcac atttctgca 120
gaaaagggtg cgggtcccat cactctcct ctcccatagc catcccagag gggtagtag 180
ccatcangcc ttcggtggga gggagtcang gaaacaacan accacagagc anacagacca 240
ntgatgacca tgggcgggag cgagcctctt ccctgnaccg ggggtggcna nganagccta 300
nctgaggggt cacactataa acgttaacga ccnagatnan cacctgcttc aagtgcaccc 360
ttcctacctg acnaccagng accnnnaact gngcctggg gacagcnctg ggancagcta 420
acnnagcact cacctgcccc cccatggcgg tncgcntccc tggctctgnc aagggaagct 480
ccctgttggg attncgggga nacaaaggga nccccctcct ccantctgtg aggaaaaann 540
gatggaattt tnccttccg gccnntcccc tcttcttcta caagccccct nntactctc 600
tccctctntt ntctgncnc acttttnacc cennnatttc ccttnattga tcggannctn 660
ganattccac tnnccctnc cntcnatcng naanacnaaa nactntctna cccnggggat 720
gggnccctcg ntcacctct cttttcnct accnccnnt ctttgctct cctngatca 780

```

tccaacnctc gntggccntn cccccccnnn tcccttnccc

820

<210> 27
 <211> 818
 <212> DNA
 <213> Homo sapien
 <220>
 <221> misc_feature
 <222> (1)... (818)
 <223> n = A,T,C or G

<400> 27
 tctgggtgat ggctcttcc tccctcaggga cctctgactg ctctgggcca aagaatctct 60
 tgtttcttct ccgagcccca ggcagcgggtg attcagccct gcccaacctg attctgatga 120
 ctgcggtatgc tgtgacggac ccaaggggca aataggggtcc cagggtccag ggagggggcgc 180
 ctgctgagca cttccgcccc tcacctgcc cagccccctgc catgagctct gggctgggtc 240
 tccgectcca gggttctgct cttccangca ngccancaag tggcgctggg ccacactggc 300
 ttcttctcgc ccntccctg gctctgante tctgtcttcc tgtcctgtgc angcnccttg 360
 gatctcagtt tccctcnctc anngaactct gtttctgann tcttcantta actntgantt 420
 tatnaccnan tggnetgtnc tgtcnnactt taatgggcn gaccggctaa tccctccctc 480
 nctcccttcc anttcnnna accngcttnc cntctctcc ccntancccg ccngggaanc 540
 ctcccttgcc ctnaccangg gccnnnaccg ccctnnctn ggggggcnng gtnnctnnc 600
 ctgntnnccc cncctcnnt tncctcgtcc cnnccnccn nngcannttc ncngtcccn 660
 tnnctcttcn ngntcgnaa ngntcnctn nnnnnngn ngntnntn tccctctcnc 720
 cnntgngang tntttnnnnc ncngnncccc nnnnnnnnn nggnntnnn tctnncngc 780
 ccnncccccc ngnattaagg cctcnnctc ccggccnc 818

<210> 28
 <211> 731
 <212> DNA
 <213> Homo sapien
 <220>
 <221> misc_feature
 <222> (1)... (731)
 <223> n = A,T,C or G

<400> 28
 aggaagggcg gagggatatt gtangggatt gagggatagg agnataangg gggagggtgtg 60
 tccaacatg anggtgnngt tctcttttga angagggttg ngtttttann ccnggtgggt 120
 gattnaaccc cattgtatgg agnnaaagg ttnagggat ttttcggctc ttatcagtat 180
 ntanattcct gtnaatcgga aaatnatntt tcnnccnggaa aatnttgctc ccatccgnaa 240
 attnctccc ggtagtgcatt ntngggggg cngccangtt tcccaggctg ctanaatcgt 300
 actaaagntt naagtgggan tncaaatgaa aacctnncc agagnatccn taccgactg 360
 tnnnttncct tcgcccctng actctgcng agcccaatac ccngngnat gtcnccngn 420
 nnngcgcnc tgaaannnnc tcgnggctnn gancatcang gggtttcgca tcaaaagcnn 480
 cgtttencat naaggcactt tngcctcacc caaccnctng ccctcncca tttngccgctc 540
 nggttencct acgctnntng cncctnnntn ganattttnc ccgctnngg naancctcct 600
 gnaatgggta gggnetntc ttttnaccnn gnggtntact aatcnnctnc acgctnctt 660
 tctnaccccc ccccttttt caatcccanc ggcnaatggg gtctccccnn cgangggggg 720
 nnccccann c 731

<210> 29
 <211> 822
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1) ... (822)
 <223> n = A,T,C or G

<400> 29
 actagtccag tgtggtggaa ttccattgtg ttggggncnc ttctatgant antnttagat 60
 cgctcanacc tcacanctc ccnacnange ctataangaa nannaataga nctgtncnnt 120
 atntntacnc tcatanncct cnnnaccac tccctcttaa cccntactgt gcctatngcn 180
 tnnctantct ntgcgcctn cnanccaccn gtgggcnac cncnngnatt ctcnatctcc 240
 tcnccatntn gcctananta ngtncatacc ctatacctac nccaatgcta nnnctaancn 300
 tccatnantt annmtaacta ccactgaant ngactttcnc atnanctcct aatttgaatc 360
 tactctgact cccacngcct annnattagc anctcccccc nacnatntct caaccaaacc 420
 ntcaacaacc tatctantctg ttccccacc nttncctccg atccccnnac aacccccctc 480
 ccaaataccc nccacctgac ncctaaccn caccatcccg gcaagccnan ggncatttan 540
 ccactggaat cacnatngga naaaaaaac ccnaactctc tancncnnat ctccctaana 600
 aatnctcctn naatttactn ncantnccat caancccaen tgaaacnnaa cccctgtttt 660
 tanatccctt ctttcgaaaa ccnaccctt annncccaac ctttngggcc ccccnctnc 720
 ccnaatgaag gncnccaat cnangaaacg nccntgaaaa ancnaaggcna anannntccg 780
 canatcctat cccctanttn ggggncctt nccngggcc cc 822

<210> 30
 <211> 787
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1) ... (787)
 <223> n = A,T,C or G

<400> 30
 cggcgcctg ctctggcaca tgccctcctga atggcatcaa aagtgatgga ctgcccattg 60
 ctagagaaga ccttctctcc tactgtcatt atggagccct gcagactgag ggctcccctt 120
 gtctgcagga tttgatgtct gaagtcgtgg agtgtggctt ggagctctc atctacatna 180
 gctggaagcc ctggagggcc tctctcgcca gcctcccct tctctccacg ctctccangg 240
 acaccagggg ctccaggcag cccattattc ccagnangac atgggtgtttc tccacgcgga 300
 cccatggggc ctgnaaggcc agggctcctt ttgacaccat ctctcccgtc ctgcctggca 360
 ggccgtggga tccactantt ctanaacggn cgccaccncg gtgggagctc cagcttttgt 420
 tccnttaat gaaggttaat tgcnegcttg gcgtaatcat nggtcanaac tntttcctgt 480
 gtgaaattgt ttntccctc ncnatccnc ncnacataen aacccggaan cataaagtgt 540
 taaagcctgg gggtngectn nngaataaac tnaactcaat taattgcgtt ggctcatggc 600
 ccgctttccn ttcnngaaaa ctgtentccc ctgcnttnt gaatcgcca ccccccnggg 660
 aaaagcgggt tgcnttttng ggggntcctt ccncttcccc cctcnctaan cctncgcct 720
 cggtcgttnc nggtngcggg gaanggnat nnnctcccnc naagggggng agnnngntat 780
 ccccaaa 822

<210> 31
 <211> 799
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1) ... (799)
 <223> n = A,T,C or G

<400> 31

```

tttttttttt tttttttggc gatgctactg ttttaattgca ggaggtgggg gtgtgtgtac      60
catgtaccag ggctattaga agcaagaagg aaggagggag gcagagcgc cctgctgagc      120
aacaaggac tcctgcagcc ttctctgtct gtctcttggc gcaggcacat ggggaggcct      180
cccgagggt gggggccacc agtccagggg tgggagcact acanggggtg ggagtgggtg      240
gtggctggtg cnaatggcct gncacanatc cctacgattc ttgacacctg gatttcacca      300
ggggaccttc tgttctccca nggnaacttc nttnatctcn aaagaacaca actgtttctt      360
cngcanttct ggctgttcat ggaaagcaca ggtgtccnat ttnggctggg acttggtaca      420
tatggttccg gcccacctct ccntcnaan aagtaattca ccccccccn cntctnttg      480
cctgggcccct taantaccca caccggaact canttanta ttcatcttng gntgggcttg      540
ntnatcnecn cctgaangcg ccaagttgaa aggccacgcc gtncccnctc cccatagnan      600
nttttnnct canctaagtc cccccnggc aacnaccaa tcccccccn tgggggcccc      660
agccanggc ccccgncctc ggnnnccngn cncgnantcc ccaggntctc ccantcngnc      720
ccnnngcncc cccgcacgca gaacanaagg ntngagccnc cgcannnnnn nggtnncnac      780
ctcgccccc cccnccgng

```

```

<210> 32
<211> 789
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(789)
<223> n = A,T,C or G

```

```

<400> 32
tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt      60
ttttncnag ggcaggttta ttgacaacct cncgggacac aancaggctg gggacaggac      120
ggcaacaggc tcggcgggcg gcggcgggcg ccctacctgc ggtaccaaat ntgcagcctc      180
cgctcccgct tgatnttccct ctgcagctgc aggatgccnt aaaacagggc ctcggccntn      240
ggtgggcacc ctgggatttn aatttccacg ggcacaatgc ggtcgcance cctcaccacc      300
nattaggaat agtggtnnta ccnccnccg ttggcncact cccentggaa accacttntc      360
gcggctccgg catctggctc taaaccttgc aaacnctggg gccctctttt tggttantnt      420
nccngccaca atcatnactc agactggcnc gggctggccc caaaaaan cncccaaaacc      480
ggncatgtc ttncgggggt tgctgcnatn tncatcacct cccgggcnca ncaggncaac      540
ccaaaagtgc ttgnggcccn caaaaaanct ccggggggnc ccagtttcaa caaagtcatc      600
ccccttggcc cccaaatcct cccccgntt nctgggttg ggaacccacg cctctnnctt      660
tggnggcaa gntgntccc ccttcgggccc cccggtgggc ccnctctaa ngaaaacncc      720
ntcctnnnca ccatcccccc nngnnacgnc tancaangna tccctttttt tanaaacggg      780
ccccccncc

```

```

<210> 33
<211> 793
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(793)
<223> n = A,T,C or G

```

```

<400> 33
gacagaacat gttggatggt ggagcacctt tctatacgac ttacaggaca gcagatgggg      60
aattcatggc tgttgagca atanaacccc agttctacga gctgctgac aaaggacttg      120
gactaaagtc tgatgaactt cccaatcaga tgagcatgga tgattggcca gaaatgaana      180
agacgtttgc agatgtattt gaaaagaaga cgaaggcaga gtggtgtcaa atctttgacg      240
gcacagatgc ctgtgtgact ccggttctga cttttgagga ggttgttcat catgatcaca      300
acaangaacg gggctcgttt atcaccantg aggagcagga cgtgagcccc cgccctgcac      360

```

ctctgctgtt	aaacacccca	gccatccctt	ctttcaaaag	ggatccacta	cttctagagc	420
ggncgccacc	gcggtggagc	tccagctttt	gttcccttta	gtgagggtta	attgcgcgct	480
tggcgtaatc	atggtcatan	ctgtttcctg	tgtgaaattg	ttatccgctc	acaattccac	540
acaacatacg	ancoggaagc	atnaaatttt	aaagcctggg	ggtngcctaa	tgantgaact	600
nactcacatt	aattggcttt	gcgctcactg	cccgctttcc	agtccggaaa	acctgtcctt	660
gccagctgcc	nttaatgaat	cnggccaccc	cccggggaaa	aggcngtttg	cttnttgggg	720
cgcncctccc	gctttctcgc	ttcctgaant	ccttcccccc	ggtctttcgg	cttgcggcna	780
acggtatcna	cct					793

<210> 34
 <211> 756
 <212> DNA
 <213> Homo sapien

 <220>
 <221> misc_feature
 <222> (1) ... (756)
 <223> n = A,T,C or G

<400> 34						
gccgcgaccg	gcatgtacga	gcaactcaag	ggcgagtggg	accgtaaaag	ccccaatctt	60
ancaagtgcg	gggaanagct	gggtcgactc	aagctagttc	ttctggagct	caacttcttg	120
ccaaccacag	ggaccaagct	gaccaaacag	cagctaattc	tggcccgtga	catactggag	180
atcggggccc	aatggagcat	cctaagcaan	gacatcccct	ccttcgagcg	ctacatggcc	240
cagctcaaat	gctactactt	tgattacaan	gagcagctcc	ccgagtcagc	ctatatgcac	300
cagctcttgg	gcctcaacct	cctcttctcg	ctgtcccaga	accgggtggc	tgantnccac	360
acgganttgg	ancggctgcc	tgcccaanga	catacanacc	aatgtctaca	tcnaccacca	420
gtgtcctgga	gcaatactga	tgganggcag	ctaccncaaa	gtnttcctgg	ccnagggtaa	480
catccccgcg	cgagagctac	accttcttca	ttgacatcct	gctcgacact	atcagggatg	540
aaaatcgong	ggttgctcca	gaaaggctnc	anaaanatcc	ttttcnctga	aggcccccg	600
atnncntagt	nctagaatcg	gcccgcacac	gcggtgganc	ctccaacctt	tcgttncctt	660
ttactgaggg	tttattgccc	cccttgccgt	tatcatggtc	acncngttt	cctgtgttga	720
aattnttaac	ccccacaaat	tccacgcena	cattnng			756

<210> 35
 <211> 834
 <212> DNA
 <213> Homo sapien

 <220>
 <221> misc_feature
 <222> (1) ... (834)
 <223> n = A,T,C or G

<400> 35						
ggggatctct	anactnacct	gnatgcatgg	ttgtcggtgt	ggtcgctgtc	gatgaanatg	60
aacaggatct	tgcccttgaa	gctctcggct	gctgtnttta	agttgctcag	tctgccgtca	120
tagtcagaca	cnetcttggg	caaaaaacan	caggatntga	gtcttgattt	cacctccaat	180
aatcttctng	gctgtctgct	cggtgaactc	gatgacnang	ggcagctggg	tgtgtntgat	240
aaantccanc	angttctcct	tggtgacctc	cccttcaaa	ttgttccggc	cttcatcaaa	300
cttctnnaan	angannancc	canctttgtc	gagctgggat	ttgganaaca	cgctactgtt	360
ggaaactgat	cccaaatggg	atgtcatcca	tcgcctctgc	tgccctgcaa	aaacttgctt	420
ggcncaaatc	cgactccccn	tccttgaaag	aagccnatca	cacccccctc	cctggactcc	480
nncaangact	ctncgcctnc	cccntccnng	cagggttggg	ggcannccgg	gcccntgcgc	540
ttcttcagcc	agttcacnat	nttcatcagc	ccctctgcca	gctgttntat	tccttggggg	600
ggaanccgtc	tctcccttcc	tgaannaact	ttgaccgtng	gaatagccgc	gcntcncnt	660
acntnctggg	ccgggttcaa	antccctccn	ttgncnntcn	cctcggggcca	ttctggattt	720
ncnnaacttt	ttccttcccc	cncctcncgg	ngtttggntt	tttcatnggg	ccccaaactct	780

gctnttggcc antcccttgg gggcntntan cccccctnt ggtcccntng ggcc

834

<210> 36
 <211> 814
 <212> DNA
 <213> Homo sapien
 <220>
 <221> misc_feature
 <222> (1) ... (814)
 <223> n = A,T,C or G

<400> 36
 cgngcgttt ccngccgccc ccggtttcca tgacnaaggg tcccttcang ttaaatacnn 60
 cctagnaaac attaatgggt tgctctacta atacatcata cnaaccagta agcctgcccc 120
 naacgccaac tcaggccatt cctaccaaag gaagaaaggg tggctctctcc acccctgta 180
 ggaaaggcct gccttgtaag acaccacaat ncggtgaat ctnaagtctt gtgttttact 240
 aatggaaaaa aaaaataaac aanaggtttt gttctcatgg ctgccaccg cagcctggca 300
 ctaaaacanc ccagcgctca cttctgcttg ganaaatatt ctttgctctt ttggacatca 360
 ggcttgatgg tatcactgcc acntttccac ccagctgggc ncccttcccc catntttgtc 420
 antganctgg aaggcctgaa ncttagtctc caaaagtctc ngcccacaag accggccacc 480
 aggggangtc ntttncagt gatctgcaa anantaccn tatcatcnnt gaataaaaag 540
 gccctgaac ganatgcttc cancanctt taagacccat aatcctngaa ccatggtgcc 600
 ctcccggtct gatccnaaag gaatgttctt gggctccant ccctcctttg ttncttacgt 660
 tgnttggac cntgtctngn atnaccaan tganatcccc ngaagcacc tnccttggc 720
 atttganttt cntaaattct ctgccctacn nctgaaagca cnattccctn ggcncnaan 780
 gngaaactca agaaggtctn ngaaaaacca cncn 814

<210> 37
 <211> 760
 <212> DNA
 <213> Homo sapien
 <220>
 <221> misc_feature
 <222> (1) ... (760)
 <223> n = A,T,C or G

<400> 37
 gcatgctgct ctctctcaaa gttgttcttg ttgccataac aaccaccata ggtaaagcgg 60
 gcgcagtgtt cgctgaaggg gttgtagtac cagcgcgga tgctctcctt gcagagtcct 120
 gtgtctggca ggtccacgca atgcccttg tcaactggga aatggatgcg ctggagctcg 180
 tcnaanccac tcgtgtattt ttcacangca gcctcctccg aagcntccgg gcagtggggg 240
 gtgtcgtcac actccactaa actgtcgatn cancagccca ttgttcgagc ggaactgggt 300
 gggctgacag gtgccagaac aactggatn ggctttcca tggaaagggc tgggggaaat 360
 cncctnancc caaactgect ctcaaaggcc accttgaca ccccgacagg ctagaatgc 420
 actcttcttc ccaaaggtag ttgttcttgt tgcccaagca ncctccanca aaccaaaanc 480
 ttgcaaaatc tgctccgtgg gggcatnnn taccanggtt ggggaaanaa acccggcngn 540
 gancncctt gtttgaatgc naaggaata atcctcctgt cttgcttggg tggaaagca 600
 caattgaact gttaacnttg ggccgngttc cncnnggtg gtctgaaact aatcacgcgc 660
 actggaaaaa ggtangtgcc ttccttgaat tcccaaantt cccctngntt tgggtntttt 720
 ctctctncc ctaaaaatcg tnttcccccc cntangggc 760

<210> 38
 <211> 724
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(724)
 <223> n = A,T,C or G

<400> 38
 tttttttttt tttttttttt tttttttttt ttttttaaaa cccctccat tgaatgaaaa 60
 cttccnaaat tgtccaaccc ctcnnccaa atnnccattt cggggggggg gttccaaacc 120
 caaattaatt ttgganttta aattaaatnt tnatnngggg aanaanccaa atgtnaagaa 180
 aatttaaccc attatnaact taaatnccn gaaacccntg gnttccaaaa atttttaacc 240
 cttaaaatccc tccgaaattg ntaanggaaa accaaattcn cctaaggctn tttgaagggt 300
 ngattttaaac ccccttnant tnttttnacc cnnngnctnaa ntatttngnt tccggtgttt 360
 tccntntaan cntnggtaac tcccngtaat gaannnccct aanccaatta aaccgaattt 420
 tttttgaatt ggaaattccn ngggaattna cgggggtttt tccnttttg ggccatncc 480
 cccnctttcg ggggttgggn ntagggtgaa tttttnnang ncccaaaaaa ncccccaana 540
 aaaaaactcc caagnnttaa ttngaattnc ccccttccca ggccttttg gaaaggnggg 600
 tttntggggg ccngggantt cnttccccn ttncncccc cccccnggt aaanggttat 660
 ngnttttggg ttttgggccc cttnanggac cttccggatn gaaattaaat ccccggngcg 720
 gccg 724

<210> 39
 <211> 751
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(751)
 <223> n = A,T,C or G

<400> 39
 tttttttttt tttttctttg ctcacattta atttttatnt tgattttttt taatgctgca 60
 caacacaata tttatttcat ttgtttcttt tatttcattt tatttgtttg ctgctgctgt 120
 tttatttatt ttactgaaa gtgagaggga acttttggtg ccttttttcc tttttctgta 180
 ggccgcctta agctttctaa atttggaaca tctaagcaag ctgaanggaa aagggggttt 240
 cgcaaaatca ctggggggaa nggaaagggt gctttgttaa tcatgcccta tgggtgggtga 300
 ttaactgctt gtacaattac ntttcacttt taattaattg tgctnaangc ttttaattana 360
 cttgggggtt ccttccccn accaaccccn ctgacaaaaa gtgccngccc tcaaatnatg 420
 tcccggcnnt cnttgaaaca cacngcngaa ngttctcatt ntccccncnc caggtnaaaa 480
 tgaagggtta ccatntttaa cncacctcc acntggcnnn gcctgaatcc tcnaaaancn 540
 cctcaancn aatnctnng ccccggtcnc gcntnngtcc cncgggggt cgggaantn 600
 cccccnga anncnntnnc naacnaaatt ccgaaaatat tccnntcnc tcaattcccc 660
 cnnagactnt ctcnncnan cncaattttc tttntntcac gaacncgnnc cnnaaatgn 720
 nnnncnctc cncnngtcn naatcnccan c 751

<210> 40
 <211> 753
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(753)
 <223> n = A,T,C or G

<400> 40
 gtggtatttt ctgtaagatc aggtgttccct ccctcgtagg tttagaggaa acaccctcat 60
 agatgaaaac ccccccgaga cagcagcact gcaactgccca agcagccggg gtaggggggg 120

cgccctatgc	acagctgggc	ccttgagaca	gcagggttc	gatgtcaggc	tcgatgtcaa	180
tggtctggaa	gcggcggctg	tacctgcgta	ggggcacacc	gtcagggccc	accaggaact	240
tctcaaagtt	ccaggcaacn	tcgttgcgac	acaccggaga	ccagggtgatn	agcttgggggt	300
cggtcataa	cgcggtggcg	tcgtcgctgg	gagctggcag	ggcctccgc	aggaaggcna	360
ataaaaggtg	cgccccgca	ccgttcant	cgcacttctc	naanaccatg	angttgggct	420
cnaaccacc	accannccg	acttccttga	nggaattccc	aaatctcttc	gntcttgggc	480
ttctnctgat	gccctanctg	gttgcccn	atgccaanca	nccccaance	ccgggggtcct	540
aaanaccen	cctcctentt	tcctctgggt	tnttntcccc	ggacntgggt	tcctctcaag	600
ggancccata	tctcnaccan	tactcacent	ncccccent	gnnaccanc	cttctanngn	660
ttccncccg	ncctctggcc	cntcaaan	gcttnacna	cctgggtctg	ccttcccccc	720
tnccctatct	gnacccn	tttgtctcan	tnt			753

<210> 41
 <211> 341
 <212> DNA
 <213> Homo sapien

<400> 41						
actatatcca	tcacaacaga	catgcttcat	cccatagact	tcttgacata	gcttcaaagt	60
agtgaacca	tccttgattt	atatacatat	atgttctcag	tattttggga	gcctttccac	120
ttctttaaac	cttggttcatt	atgaacactg	aaaataggaa	tttgtaaga	gttaaaaagt	180
tatagcttgt	ttacgtagta	agtttttgaa	gtctacattc	aatccagaca	cttagttgag	240
tggttaaactg	tgatttttaa	aaaatatcat	ttgagaatat	tctttcagag	gtattttcat	300
ttttactttt	tgattaattg	tgttttatat	attagggtag	t		341

<210> 42
 <211> 101
 <212> DNA
 <213> Homo sapien

<400> 42						
acttactgaa	tttagttctg	tgctcttctt	tatttagtgt	tgtatcataa	atactttgat	60
gtttcaaaca	ttctaaataa	ataattttca	gtggcttcat	a		101

<210> 43
 <211> 305
 <212> DNA
 <213> Homo sapien

<400> 43						
acatctttgt	tacagtctaa	gatgtgttct	taaatcacca	ttccttctctg	gtcctcacc	60
tccaggggtg	tctcacactg	taattagagc	tattgaggag	tctttacagc	aaattaagat	120
tcagatgcct	tgctaagtct	agagttctag	agttatgttt	cagaaagtct	aagaaacca	180
cctcttgaga	ggtcagtaaa	gaggacttaa	tatttcatat	ctacaaaatg	accacaggat	240
tgatacaga	acgagagtta	tcctggataa	ctcagagctg	agtacctgcc	cgggggccgc	300
tcgaa						305

<210> 44
 <211> 852
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(852)
 <223> n = A,T,C or G

<400> 44

acataaatat	cagagaaaag	tagtctttga	aatatttacg	tccaggagtt	ctttgtttct	60
gattatttgg	tgtgtgtttt	ggtttgtgtc	caaagtattg	gcagcttcag	ttttcatttt	120
ctctccatcc	tcgggcattc	ttcccaaatt	tatataccag	tcttcgtcca	tccacacgct	180
ccagaatttc	tctttttag	taatattctca	tagctcggct	gagcttttca	taggtcatgc	240
tgctgttgtt	cttcttttta	ccccatagct	gagccactgc	ctctgatttc	aagaacctga	300
agacgccctc	agatcggctc	tcccatttta	ttaatcctgg	gttcttgtct	gggttcaaga	360
ggatgtcgcg	gatgaattcc	cataagttag	tccctctcgg	gttgtgcttt	ttggtgtggc	420
acttggcagg	ggggtcttgc	tcctttttca	tatcagggtga	ctctgcaaca	ggaagggtgac	480
tggtggttgt	catggagatc	tgagcccggc	agaaagtttt	gctgtccaac	aaatctactg	540
tgctaccata	gttggtgtca	tataaatagt	tctngtcttt	ccagggtgtc	atgatggaag	600
gctcagtttg	ttcagtcctg	acaatgacat	tgtgtgtgga	ctggaacagg	tcactactgc	660
actggccgtt	ccacttcaga	tgctgcaagt	tgctgtagag	gagntgcccc	gccgtccctg	720
ccgcccgggt	gaactcctgc	aaactcatgc	tgcaaagggtg	ctcgccgttg	atgtcgaact	780
cntggaaagg	gatacaattg	gcatccagct	ggttgggtgc	caggaggtga	tggagccact	840
cccacacctg	gt					852

<210> 45
 <211> 234
 <212> DNA
 <213> Homo sapien

<400> 45	
acaacagacc	cttgctcgct aacgacctca tgctcatcaa gttggacgaa tccgtgtccg 60
agctcgacac	catccggagc atcagcattg cttcgcagtg ccctaccgcg gggaaactctt 120
gcctcgtttc	tggtgggggt ctgctggcga acggcagaaat gcctaccgtg ctgcaagtgcg 180
tgaacgtgtc	ggtggtgtct gaggaggtct gcagtaagct ctatgaccgg ctgt 234

<210> 46
 <211> 590
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1) ... (590)
 <223> n = A,T,C or G

<400> 46	
actttttatt	taaatgttta taaggcagat ctatgagaat gatagaaaac atggtgtgta 60
atttgatagc	aatatttttg agattacaga gttttagtaa ttaccaatta cacagttaaa 120
aagaagataa	tatattccaa gcanatacaa aatatctaata gaaagatcaa ggcaggaaaa 180
tgantataac	taattgacaa tggaaaatca attttaattgt gaattgcaca ttatccttta 240
aaagctttca	aaanaaanaa ttattgcagt ctanttaatt caaacagtgt taaatgggtat 300
caggataaan	aactgaaggg canaaagaat taattttcac ttcattgtaac ncacccanat 360
ttacaatggc	ttaaatgcan ggaaaaagca gtggaagtag ggaagtantc aaggtctttc 420
tggtctctaa	tctgccttac tctttgggtg tggccttgat cctctggaga cagctgccag 480
ggctcctgtt	atatccacaa tcccagcagc aagatgaagg gatgaaaaag gacacatgct 540
gccttccttt	gaggagactt catctcactg gccaacactc agtcacatgt 590

<210> 47
 <211> 774
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1) ... (774)
 <223> n = A,T,C or G

```

<400> 47
acaagggggc ataatgaagg agtgggggana gatttttaag aaggaaaaaa aacgaggccc      60
tgaacagaat tttcctgnac aacgggggctt caaaataatt ttcttgggga gggtcaagac      120
gcttcactgc ttgaaactta aatggatgtg ggacanaatt ttctgtaatg accctgaggg      180
cattacagac gggactctgg gaggaaggat aaacagaaag gggacaaagg ctaatcccaa      240
aacatcaaag aaaggaagggt ggcgtcatat ctcccagcct acacagttct ccagggtctct      300
cctcatccct ggaggacgac agtggaggaa caactgacca tgtccccagg ctctgtgtg      360
ctggtctctg gtcttcagcc cccagctctg gaagcccacc ctctgtgat cctgcgtggc      420
ccacactcct tgaacacaca tccccaggtt atattcctgg acatggctga acctcctatt      480
cctacttccg agatgccttg ctccctgcag cctgtcaaaa tcccactcac cctccaaacc      540
acggcatggg aagcctttct gacttgctg attactccag catcttggaa caatccctga      600
ttccccactc cttagaggca agataggggtg gtttaagagta gggctggacc acttgagacc      660
aggctgctgg cttcaaattn tggctcattt acgagctatg ggaccttggg caagtnatct      720
tcacttctat gggcntcatt ttgttctacc tgcaaaatgg gggataataa tagt          774

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```

<210> 48
<211> 124
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(124)
<223> n = A,T,C or G

```

```

<400> 48
canaaattga aattttataa aaaggcattt ttctettata tccataaaat gatataattt      60
ttgcaantat anaaatgtgt cataaattat aatgttcctt aattacagct caacgcaact      120
tggt                                              124

```

```

<210> 49
<211> 147
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(147)
<223> n = A,T,C or G

```

```

<400> 49
gccgatgcta ctattttatt gcaggagggtg ggggtgtttt tattattctc tcaacagctt      60
tgtggctaca ggtggtgtct gactgcatna aaaanttttt tacgggtgat tgcaaaaatt      120
ttagggcacc catatcccaa gcantgt                    147

```

```

<210> 50
<211> 107
<212> DNA
<213> Homo sapien

```

```

<400> 50
acattaaatt aataaaagga ctgttgggggt tctgctaaaa cacatggctt gatatatatgc      60
atgggtttgag gttaggagga gttaggcata tgttttggga gaggggt                    107

```

```

<210> 51
<211> 204
<212> DNA

```

<213> Homo sapien

<400> 51

gtcctaggaa gtctagggga cacacgactc tggggtcacg gggccgacac acttgcaagg	60
cgggaaggaa aggcagagaa gtgacaccgt cagggggaaa tgacagaaag gaaaatcaag	120
gccttgcaag gtcagaaagg ggactcaggg cttccaccac agccctgccc cacttgcca	180
cctccctttt gggaccagca atgt	204

<210> 52

<211> 491

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(491)

<223> n = A,T,C or G

<400> 52

acaagataa catttatctt ataacaaaaa tttgatagtt ttaaaggtta gtattgtgta	60
gggtattttt caaaagacta aagagataac tcaggtaaaa agttagaaat gtataaaaca	120
ccatcagaca ggttttttaa aaacaacata ttacaaaatt agacaatcat ctttaaaaaa	180
aaaacttctt gtatcaattt cttttgttca aaatgactga ctttaantatt tttaaatatt	240
tcanaaacac ttectcaaaa attttcaana tggtagcttt canatgtnc ctcagtccca	300
atgttgctca gataaataaa tctcgtgaga acttaccacc caccacaagc tttctggggc	360
atgcaacagt gtcttttctt tnccttttct tttttttttt ttacaggcac agaaactcat	420
caattttatt tggataacaa agggctctca aatttatattg aaaaataaat ccaagttaat	480
atcactcttg t	491

<210> 53

<211> 484

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(484)

<223> n = A,T,C or G

<400> 53

acataattta gcagggctaa ttaccataag atgctattta ttaanaggtn tatgatctga	60
gtattaacag ttgctgaagt ttggattttt tatgcagcat tttctttttg ctttgataac	120
actacagaac ccttaaggac actgaaaatt agtaagtaaa gttcagaaac attagctgct	180
caatcaaate tctacataac actatagtaa ttaaaacggt aaaaaaaagt gttgaaatct	240
gcactagtat anaccgctcc tgtcaggata anactgcttt ggaacagaaa gggaaaaanc	300
agctttgant ttctttgtgc tgatangagg aaaggctgaa ttaccttgtt gcctctccct	360
aatgattggc aggtcnggta aatnccaaaa catattccaa ctcaacactt cttttccncg	420
tancttgant ctgtgtattc caggancagg cggatggaat gggccagccc ncggatgttc	480
cant	484

<210> 54

<211> 151

<212> DNA

<213> Homo sapien

<400> 54

actaaacctc gtgcttgtga actccatata gaaaacgggt ccatccctga acacggctgg	60
ccactgggta tactgtctgac aaccgcaaca aaaaaaacac aaatccttgg cactggctag	120

tctatgtcct ctcaagtgcc tttttgtttg t 151

<210> 55
 <211> 91
 <212> DNA
 <213> Homo sapien

<400> 55
 acctggcttg tctccgggtg gttcccggcg ccccccacgg tccccagaac ggacactttc 60
 gccctccagt ggatactcga gccaaagtgg t 91

<210> 56
 <211> 133
 <212> DNA
 <213> Homo sapien

<400> 56
 ggccgatgtg cgttggttat atacaaatat gtcattttat gtaagggact tgagtatact 60
 tggatttttg gtatctgtgg gttgggggga cggtcagga accaataccc catggatacc 120
 aagggacaac tgt 133

<210> 57
 <211> 147
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(147)
 <223> n = A,T,C or G

<400> 57
 actctggaga acctgagccg ctgctccgcc tctgggatga ggtgatgcan gcngtggcgc 60
 gactgggagc tgagcccttc cctttgcgcc tgcctcagag gattgttgcc gacntgcana 120
 tctcantggg ctggatncat gcagggt 147

<210> 58
 <211> 198
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(198)
 <223> n = A,T,C or G

<400> 58
 acagggatat aggtttnaag ttattgtnat tgtaaaatac attgaatttt ctgtatactc 60
 tgattacata catttaccct ttaaaaaaga tgtaaatctt aatttttatg ccatctatta 120
 atttaccaat gagttacctt gtaaatgaga agtcatgata gcactgaatt ttaactagtt 180
 ttgacttcta agtttggt 198

<210> 59
 <211> 330
 <212> DNA
 <213> Homo sapien

<400> 59

acaacaaatg gggtgtgagg aagtcttatac agcaaaactg gtgatggcta ctgaaaagat	60
ccattgaaaa ttatcattaa tgattttaaa tgacaagtta tcaaaaactc actcaatddd	120
cacctgtgct agcttgctaa aatgggagtt aactctagag caaatatagt atcttctgaa	180
tacagtcaat aaatgacaaa gccagggcct acaggtgggt tccagacttt ccagaccag	240
cagaaggaat ctatdddtaac acatggatct ccgtctgtgc tcaaaaatacc taatgatatt	300
tttctgtcttt attggaacttc tttgaagagt	330

<210> 60

<211> 175

<212> DNA

<213> Homo sapien

<400> 60

accgtgggtg ccttctacat tcttgacggc tcttccacca acatctgggt ctacttcggc	60
gtcgtgggtc ccttctctt catctcctc cagctgggtc tgctcatcga ctttgccgac	120
tcttggaacc agcgggtggct gggcaaggcc gaggagtgcg attcccggtc ctggt	175

<210> 61

<211> 154

<212> DNA

<213> Homo sapien

<400> 61

acccacttt tcttctgtg agcagtctgg acttctcact gctacatgat gaggtgagt	60
gggtgtgtgct cttcaacagt atcctccctt ttccggtatc gctgagccgg acagcagtgc	120
tggactgcac agccccgggg ctccacattg ctgt	154

<210> 62

<211> 30

<212> DNA

<213> Homo sapien

<400> 62

cgctcgagcc ctatagttag tcgtattaga	30
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<210> 63

<211> 89

<212> DNA

<213> Homo sapien

<400> 63

acaagtcatt tcagaccct ttgctcttca aaactgacca tcttttatat ttaatgcttc	60
ctgtatgaat aaaaatgggt atgtcaagt	89

<210> 64

<211> 97

<212> DNA

<213> Homo sapien

<400> 64

accggagtaa ctgagtcggg acgtgaatc tgaatccacc aataaataaa ggttctgcag	60
aatcagtgc tccaggattg gtcttggat ctgggggt	97

<210> 65

<211> 377

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (377)

<223> n = A,T,C or G

<400> 65

acaacaanaa ntcccttctt taggcactg atggaaacct ggaacccccct tttgatggca	60
gcatggcgctc ctaggccttg acacagcggc tgggggtttgg gctntcccaa accgcacacc	120
ccaaccttg tctaccaca nttctggcta tgggctgtct ctgccactga acatcagggt	180
tcggtcataa natgaaatcc caanggggac agaggtcagt agaggaagct caatgagaaa	240
ggtgctgttt gctcagccag aaaacagctg cctggcattc gccgctgaac tatgaacccg	300
tgggggtgaa ctaccccan gaggaatcat gcctgggcga tgcaanggtg ccaacaggag	360
gggcgggagg agcatgt	377

<210> 66

<211> 305

<212> DNA

<213> Homo sapien

<400> 66

acgcctttcc ctcagaattc agggaagaga ctgtcgctg ccttcctccg ttgttgctg	60
agaaccgctg tgccccttc caccatatcc accctcgctc catctttgaa ctcaaacacg	120
aggaactaac tgcaccttg tctctcccc agtcccagc tcacctoca tccctcacct	180
tctccactc taagggatat caacactgcc cagcacagg gccctgaatt tatgtggtt	240
ttatatattt tttaataaga tgcactttat gtcattttt aataaagtct gaagaattac	300
tgttt	305

<210> 67

<211> 385

<212> DNA

<213> Homo sapien

<400> 67

actacacaca ctccacttgc ccttgtaga cactttgtcc cagcacttta ggaatgctga	60
ggtcggacca gccacatctc atgtgcaaga ttgccagca gacatcaggt ctgagagttc	120
cccttttaaa aaaggggact tgcttaaaaa agaagtctag ccacgattgt gtagagcagc	180
tgtgctgtgc tggagattca cttttgagag agttctcctc tgagacctga tctttagagg	240
ctgggcagtc ttgcacatga gatggggctg gtctgatctc agcactcctt agtctgcttg	300
cctctcccag ggccccagcc tggccacacc tgcttacagg gcactctcag atgccatac	360
catagtttct gtgtagtg accgt	385

<210> 68

<211> 73

<212> DNA

<213> Homo sapien

<400> 68

acttaaccag atatattttt accccagatg gggatattct ttgtaaaaaa tgaaaataaa	60
gtttttttaa tgg	73

<210> 69

<211> 536

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (536)

<223> n = A,T,C or G

<400> 69

actagtcacg	tgtggtggaa	ttccattgtg	ttgggggctc	tcaccctcct	ctcctgcagc	60
tccagctttg	tgctctgcct	ctgaggagac	catggcccag	catctgagta	ccctgctgct	120
cctgctggcc	accctagctg	tggccctggc	ctggagcccc	aaggaggagg	ataggataat	180
cccggtggc	atctataacg	cagacctcaa	tgatgagtgg	gtacagcgtg	cccttcaact	240
cgccatcagc	gagtataaca	aggccaccaa	agatgactac	tacagacgtc	cgctgcgggt	300
actaagagcc	aggcaacaga	ccgttggggg	ggtgaattac	ttcttcgacg	tagaggtggg	360
ccgaaccata	tgtaccaagt	cccagcccaa	cttggacacc	tgtgccttcc	atgaacagcc	420
agaactgcag	aagaaacagt	tgtgctcttt	cgagatctac	gaagttccct	ggggagaaca	480
gaangtcctc	gggtgaaatc	caggtgtcaa	gaaatcctan	ggatctgttg	ccaggc	536

<210> 70

<211> 477

<212> DNA

<213> Homo sapien

<400> 70

atgaccccta	acagggggcc	tctcagccct	cctaataacc	tccggcctag	ccatgtgatt	60
tcacttccac	tccataacgc	tcctcatact	aggcctacta	accaacacac	taaccatata	120
ccaatgatgg	cgcgatgtaa	cacgagaaag	cacataccaa	ggccaccaca	caccacctgt	180
ccaaaaaggc	cttcgatacg	ggataatcct	atttattacc	tcagaagtgt	ttttcttcgc	240
agggattttt	ctgagccttt	taccactcca	gcctagcccc	taccccccaa	ctaggagggc	300
actggccccc	aacaggcatc	accccgctaa	atccccctaga	agtccctact	ctaaacacat	360
ccgtattact	cgcatcagga	gtatcaatca	cctgagctca	ccatagtcta	atagaaaaca	420
accgaaacca	aattattcaa	agcactgctt	attacaattt	tactgggtct	ctattttt	477

<210> 71

<211> 533

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (533)

<223> n = A,T,C or G

<400> 71

agagctatag	gtacagtgtg	atctcagctt	tgcaaacaca	ttttctacat	agatagtact	60
aggtattaat	agatatgtaa	agaaagaaat	cacaccatta	ataatggtaa	gattgggtta	120
tgtgatttta	gtggtatttt	tggcaccctt	atataatgtt	tccaaacttt	cagcagtgat	180
attatttcca	taacttaaaa	agtgaatttg	aaaaagaaaa	tctccagcaa	gcatctcatt	240
taaaataaag	tttgtcatct	ttaaaaaatac	agcaatatgt	gactttttta	aaaagctgtc	300
aaataggtgt	gaccctacta	ataattatta	gaaatacatt	taaaaacatc	gagtacctca	360
agtcagtttg	ccttgaaaaa	tatcaaatat	aactcttaga	gaaatgtaca	taaaagaatg	420
cttcgtaatt	ttggagtang	aggttccctc	ctcaattttg	tattttttaa	aagtacatgg	480
taaaaaaaaa	aattcacaac	agtatataag	gctgtaaaaa	gaagaattct	gcc	533

<210> 72

<211> 511

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (511)

<223> n = A,T,C or G

<400> 72

tattacggaa	aaacacacca	cataattcaa	ctancaaaga	anactgcttc	agggcgtgta	60
aaatgaaagg	cttccaggca	gttatctgat	taaagaacac	taaaagagg	acaaggctaa	120
aagccgcagg	atgtctacac	tatancaggc	gctatttggg	ttggctggag	gagctgtgga	180
aaacatggan	agattgggtc	tgganatcgc	cgtggctatt	cctcattgtt	attacanagt	240
gaggttctct	gtgtgcccac	tggtttgaaa	accgttctnc	aataatgata	gaatagtaca	300
cacatgagaa	ctgaaatggc	ccaaaccag	aaagaaagcc	caactagatc	ctcagaanac	360
gcttctaggg	acaataaccg	atgaagaaaa	gatggcctcc	ttgtgcccc	gtctgttatg	420
atttctctcc	attgcagcna	naaacccgtt	cttctaagca	aacncagggtg	atgatggcna	480
aaatacaccc	cctcttgaag	naccnggagg	a			511

<210> 73

<211> 499

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (499)

<223> n = A,T,C or G

<400> 73

cagtgccagc	actggtgcca	gtaccagtac	caataacagt	gccagtgcc	gtgccagcac	60
cagtgggtgc	ttcagtgtg	gtgccagcct	gaccgccact	ctcacatttg	ggctcttcgc	120
tggccttggt	ggagctgggt	ccagcaccag	tggcagctct	gggtgcctgtg	gtttctccta	180
caagttagat	tttagatatt	gttaatcctg	ccagtcttct	tcttcaagcc	aggggtgcatc	240
ctcagaaacc	tactcaacac	agcactctag	gcagccacta	tcaatcaatt	gaagttgaca	300
ctctgcatta	aatctatttg	ccatttctga	aaaaaaaaaa	aaaaaaagg	cggccgctcg	360
antctagagg	gcccgtttta	acccgctgat	cagcctcgac	tgtgccttct	anttgccagc	420
catctgttgt	ttgcccctcc	cccngtgcct	tccttgaccc	tggaaagtgc	cactcccact	480
gtcctttcct	aantaaaat					499

<210> 74

<211> 537

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (537)

<223> n = A,T,C or G

<400> 74

tttcatagga	gaacacactg	aggagatact	tgaagaattt	ggattcagcc	gcgaagagat	60
ttatcagctt	aactcagata	aaatcattga	aagtaataag	gtaaaagcta	gtctctaact	120
tccaggccca	cggctcaagt	gaatttgaat	actgcattta	cagtgtagag	taacacataa	180
cattgtatgc	atggaaacat	ggaggaacag	tattacagtg	tcctaccact	ctaatcaaga	240
aaagaattac	agactctgat	tctacagtga	tgattgaatt	ctaaaaatgg	taatcattag	300
ggcttttgat	ttataanact	ttgggtactt	atactaaatt	atggtagtta	tactgccttc	360
cagtttgctt	gatataattg	ttgatattaa	gattcttgac	ttatattttg	aatgggttct	420
actgaaaaan	gaatgatata	ttcttgaaga	catcgatata	catttattta	cactcttgat	480
tctacaatgt	agaaaatgaa	ggaaatgccc	caaattgtat	ggtgataaaa	gtcccgt	537

<210> 75

<211> 467

<212> DNA

<213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(467)
 <223> n = A,T,C or G

<400> 75
 caaanacaat tgggtcaaaag atgcaaatga tacactactg ctgcagctca caaacacctc 60
 tgcattattac acgtacctcc tctgtctcct caagtagtgt ggtctatattt gccatcatca 120
 cctgctgtct gcttagaaga acggctttct gctgcaangg agagaaatca taacagacgg 180
 tggcacaagg aggccatctt ttctcatcg gttattgtcc ctagaagcgt cttctgagga 240
 tctagttggg ctttctttct gggtttgggc catttcantt ctcattgtgtg tactattcta 300
 tcattattgt ataacgggtt tcaaaccngt gggcacncag agaacctcac tctgtaataa 360
 caatgaggaa tagccacggg gatctccagc accaaatctc tccatgttnt tccagagctc 420
 ctccagccaa cccaatagc cgctgctatn gtgtagaaca tccctgn 467

<210> 76
 <211> 400
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(400)
 <223> n = A,T,C or G

<400> 76
 aagctgacag cattcgggcc gagatgtctc gctccgtggc cttagctgtg ctgcgctac 60
 tctctctttc tggcctggag gctatccagc gtactccaaa gattcagggt tactcacgtc 120
 atccagcaga gaattggaaa tcaaatttcc tgaattgcta tgtgtctggg tttcatccat 180
 ccgacattga agttgactta ctgaagaatg gagagagaat tgaaaaagt gagcattcag 240
 acttgtcttt cagcaaggac tggctcttct atctcttgta ctacactgaa ttcaccccca 300
 ctgaaaaaga tgagtatgcc tgccgtgtga accatgtgac tttgtcacag cccaagatng 360
 ttnagtggga tcganacatg taagcagcan catggggagg 400

<210> 77
 <211> 248
 <212> DNA
 <213> Homo sapien

<400> 77
 ctggagtgcc ttggtgtttc aagcccctgc aggaagcaga atgcaccttc tgaggcacct 60
 ccagctgccc cggcggggga tgcgaggctc ggagcaccct tgcccggctg tgattgctgc 120
 caggcactgt tcatctcagc ttttctgtcc ctttgtctcc ggcaagcgt tctgctgaaa 180
 gttcatatct ggagcctgat gtcttaacga ataaagggtc catgctccac ccgaaaaaaa 240
 aaaaaaaa 248

<210> 78
 <211> 201
 <212> DNA
 <213> Homo sapien

<400> 78
 actagtccag tgtggtggaa ttccattgtg ttgggcccac cacaatggct acctttaaca 60
 tcaccagac cccgcctgc ccgtgcccac cgctgctgct aacgacagta tgatgcttac 120
 tctgtactc ggaaactatt tttatgtaat taatgtatgc tttcttgttt ataaatgcct 180
 gatttaaaaa aaaaaaaaaa a 201

<210> 79
 <211> 552
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)... (552)
 <223> n = A,T,C or G

<400> 79
 tccttttgggt aggtttttga gacaacccta gacctaaact gtgtcacaga cttctgaatg 60
 tttaggcagt gctagtaatt tcctcgtaat gattctgtta ttactttcct attcctttatt 120
 cctctttcct ctgaagatta atgaagttga aaattgaggt ggataaatac aaaaaggtag 180
 tgtgatagta taagtatcta agtgcagatg aaagtgtgtt atatatatcc attcaaaatt 240
 atgcaagtta gtaattactc agggttaact aaattacttt aatatgctgt tgaacctact 300
 ctgttccttg gctagaaaaa attataaaca ggactttgtt agtttgggaa gccaaattga 360
 taatattcta tgttctaaaa gttgggctat acataaanta tnaagaaata tggaatttta 420
 ttcccaggaa tatgggggtc atttatgaat antaccggg anagaagttt tgantnaaac 480
 cngttttgggt taatacgtta atatgtcctn aatnaacaag gcntgactta tttccaaaaa 540
 aaaaaaaaaa aa 552

<210> 80
 <211> 476
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)... (476)
 <223> n = A,T,C or G

<400> 80
 acagggattt gagatgctaa ggccccagag atcgtttgat ccaaccctct tattttcaga 60
 ggggaaaaatg gggcctagaa gttacagagc atctagctgg tgcgctggca cccctggcct 120
 cacacagact cccgagtagc tgggactaca ggcacacagt cactgaagca ggcctgttt 180
 gcaattcacg ttgccacctc caacttaaac attcttcata tgtgatgtcc ttagtacta 240
 aggttaaaact tttccacca gaaaaggcaa cttagataaa atcttagagt actttcatac 300
 ttttctaagt cctcttccag cctcactttg agtcctcctt ggggggtgat aggaantntc 360
 tcttggtttt ctcaataaaa tctctatcca tctcatgtt aatttggtac gcntaaaaat 420
 gctgaaaaaa ttaaaatggt ctggtttcnc tttaaaaaaa aaaaaaaaaa aaaaaa 476

<210> 81
 <211> 232
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)... (232)
 <223> n = A,T,C or G

<400> 81
 tttttttttg tatgcntcn ctgtgnggtt attgttgctg ccaccctgga ggagcccagt 60
 ttctttctgta tttttctttt ctgggggatc ttctggctc tgcccccca tttccagcct 120
 ctcacccca tcttgactt ttgctagggt tggaggcgt ttctggttag cccctcagag 180
 actcagtcag cgggaataag tcttaggggt ggggggtgtg gcaagccggc ct 232

<210> 82
 <211> 383
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1) ... (383)
 <223> n = A,T,C or G

<400> 82
 aggcgggagc agaagctaaa gccaaagccc aagaagagtg gcagtgccag cactgggtgcc 60
 agtaccagta ccaataacat gccagtgccg gtgccagcac cagtgggtggc ttcagtgtctg 120
 gtgccagcct gaccgccact ctacatattg ggctcttcgc tggccttggg ggagctgggtg 180
 ccagcaccag tggcagctct ggtgcctgtg gtttctccta caagtgagat tttagatatt 240
 gttaatcctg ccagtctttc tcttcaagcc aggggtgcac ctcaaaaacc tactcaacac 300
 agcactctng gcagccacta tcaatcaatt gaagttgaca ctctgcatta aatctatttg 360
 ccatttcaaa aaaaaaaaaa aaa 383

<210> 83
 <211> 494
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1) ... (494)
 <223> n = A,T,C or G

<400> 83
 accgaattgg gaccgtggc ttataagcga tcatgtcttc cagtattacc tcaacgagca 60
 gggagatcga gtctatacgc tgaagaaatt tgaccgatg ggacaacaga cctgtctcagc 120
 ccattcctgct cggttctccc cagatgacaa atactctcga caccgaatca ccatcaagaa 180
 acgtttcaag gtgtcatga cccagcaacc gcgccctgtc ctctgagggt ccttaaactg 240
 atgtcttttc tgccacctgt taccctctcg agactccgta accaaactct tcggactgtg 300
 agccctgatg cctttttgccc agccatactc tttggcntcc agtctctcgt ggcgattgat 360
 tatgcttggtg tgaggcaatc atggtggcat caccatnaa gggaacacat ttganttttt 420
 tttncatat tttaaattac naccagaata nttcagaata aatgaattga aaaactctta 480
 aaaaaaaaaa aaaa 494

<210> 84
 <211> 380
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1) ... (380)
 <223> n = A,T,C or G

<400> 84
 gctggtagcc tatggcgtgg ccacggangg gtcctgagg cacgggacag tgacttccca 60
 agtatcctgc gccgcgtctt ctaccgtccc tacctgcaga tcttcgggca gattccccag 120
 gaggacatgg acgtggccct catggagcac agcaactgct cgtcggagcc cggcttctgg 180
 gcacaccctc ctggggccca ggcgggcacc tgcgtctccc agtatgccaa ctggctgggtg 240
 gtgctgtctc tctcatctt cctgctcgtg gccaacatcc tgctgggtcac ttgctcattg 300
 ccatgttcag ttacacattc ggcaaagtac agggcaacag cnatctctac tgggaaggcc 360
 agcgttnccg cctcatccgg 380

<210> 85
 <211> 481
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(481)
 <223> n = A,T,C or G

<400> 85
 gagttagctc ctccacaacc ttgatgaggt cgtctgcagt ggccctctcgc ttcataaccgc 60
 tnccatcgctc atactgtagg tttgccacca cctcctgcat cttggggcgg ctaatatcca 120
 ggaaactctc aatcaagtca ccgtcnatna aacctgtggc tggttctgtc ttccgctcgg 180
 tgtgaaagga tctccagaag gagtgtctga tcttcccac acttttgatg actttattga 240
 gtcgattctg catgtccagc aggaggttgt accagctctc tgacagtga gtcaccagcc 300
 ctatcatgcc nttgaacgtg ccgaagaaca ccgagccttg tgtggggggg gnagtctcac 360
 ccagattctg cattaccaga nagccgtggc aaaaganatt gacaactcgc ccaggngaa 420
 aaagaacacc tcttggaagt gctngccgct cctcgtcnt tgggtggngc gcntnccttt 480
 t 481

<210> 86
 <211> 472
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(472)
 <223> n = A,T,C or G

<400> 86
 aacatcttcc tgtataatgc tgtgtaatat cgatccgatn ttgtctgctg agaattcatt 60
 acttgaaaa gcaacttnaa gcctggacac tggattataa attcacaata tgcaacactt 120
 taacacgtgt gtcaatctgc tcccttactt tgtcatcacc agtctgggaa taagggtatg 180
 cctattcac acctgtttaa agggcgctaa gcatttttga ttcaacatct tttttttga 240
 cacaagtcgg aaaaaagcaa aagtaaacag ttnttaattt gttagccaat tcactttctt 300
 catgggacag agccatttga tttaaaaagc aaattgcata atattgagct ttgggagctg 360
 atatntgagc ggaagantag cctttctact tcaccagaca caactcctt catattggga 420
 tgttnacnaa agttatgtct cttacagatg ggatgctttt gtggcaattc tg 472

<210> 87
 <211> 413
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(413)
 <223> n = A,T,C or G

<400> 87
 agaaaccagt atctctnaaa acaacctctc ataccttggtg gacctaatTT tgtgtgcgtg 60
 tgtgtgtgcg cgcataattat atagacaggc acatcttttt tacttttgta aaagcttatg 120
 cctctttggt atctatatct gtgaaagttt taatgatctg ccataatgtc ttggggacct 180
 ttgtcttctg tgtaaagtgt actagagaaa acacctatnt tatgagtcaa tctagttngt 240
 tttattcgac atgaaggaaa tttccagatn acaacactna caaactctcc cttgactagg 300

ggggacaaag aaaagcanaa ctgaacatna gaaacaattn cctggtgaga aattncataa 360
acagaaattg ggtngtatat tgaaanang catcattnaa acgttttttt ttt 413

<210> 88
<211> 448
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(448)
<223> n = A,T,C or G

<400> 88
cgcagcgggt cctctctatc tagtccagc ctctcgctg cccactccc cgcgtcccgc 60
gtcctagccn accatggccg ggeccctgcg cgcccgcgtg ctctgctgg ccatcctggc 120
cgtggccctg gcggtgagcc ccgcgcccg ctccagtccc ggcaagccgc cgcgcctggt 180
gggaggccca tggaccccg gtggaagaag aaggtgtgcg gcggtgactg gactttgccg 240
tcggcnanta caacaaacc gcaacnactt ttaccnagcn cgcgtgcag gttgtgccgc 300
cccaancaaa ttgttactng gggtaantaa ttcttggaag ttgaacctgg gccaaacnng 360
tttaccagaa ccnagccaat tngaacaatt ncccctccat aacagcccct tttaaaaagg 420
gaancantcc tgnctctttc caaat ttt 448

<210> 89
<211> 463
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(463)
<223> n = A,T,C or G

<400> 89
gaattttgtg cactggccac tgtgatggaa ccattgggcc aggatgcttt gagtttatca 60
gtagtgttc tgccaaagt ggtgttgtaa catgagtatg taaaatgtca aaaaattagc 120
agaggtctag gtctgcatat cagcagacag ttgtccgtg tattttgtag ccttgaagtt 180
ctcagtgaca agttnnttct gatgcgaagt tctnatcca gtgttttagt cctttgcatc 240
tttnatgttn agacttgcc ctntnaaatt gcttttgtnt tctgcaggta ctatctgtgg 300
tttaacaaaa tagaannact tctctgcttn gaanattga atatcttaca tctnaaaatn 360
aattctctcc ccatannaaa acccangccc ttggganaat ttgaaaaang gntccttcnn 420
aattcnnana anttcagtn tcatacaaca naacngganc ccc 463

<210> 90
<211> 400
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(400)
<223> n = A,T,C or G

<400> 90
agggattgaa ggtctntnt actgtcggac tgttcancca ccaactctac aagttgctgt 60
cttccactca ctgtctgtaa gcntnttaac ccagactgta tcttcataaa tagaacaat 120
tcttcaccag tcacatcttc taggaccttt ttggattcag ttagtataag ctctccact 180
tcctttgtta agacttcac tggtaaagtc ttaagtttg tagaaaggaa ttttaattgct 240

cgttctctaa caatgtcctc tccttgaagt atttggtga acaaccacc tnaagtcct	300
ttgtgcatcc attttaata tacttaataag ggcattggtg cactaggtta aattctgcaa	360
gagtcactcg tctgcaaaag ttgcgttagt atatctgcca	400

<210> 91
 <211> 480
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(480)
 <223> n = A,T,C or G

<400> 91	
gagctcggat ccaataatct ttgtctgagg gcagcacaca tatncagtgc catggnaact	60
gggtctacccc acatgggagc agcatgccgt agntatataa ggtcattccc tgagtcagac	120
atgcctcttt gactaccgtg tgccagtgtc ggtgattctc acacacctcc nncgctctt	180
tgtggaaaaa ctggcacttg nctggaacta gcaagacatc acttacaat tcaccacga	240
gacactgaa aggtgtaaca aagcgactct tgcattgctt tttgtccctc cggcaccagt	300
tgtcaatact aacccgctgg tttgectcca tcacatttgt gatctgtagc tctggataca	360
tctctgaca gtactgaaga acttcttctt ttgtttcaa agcaactctt ggtgcctgtt	420
ngatcagggt cccatttccc agtcggaatg ttcacatggc atatnttact tcccacaaaa	480

<210> 92
 <211> 477
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(477)
 <223> n = A,T,C or G

<400> 92	
atacagccca natcccacca cgaagatgcg cttgttgact gagaacctga tgcggtcact	60
gggtcccgctg tagccccagc gactctccac ctgctggaag cggttgatgc tgcactcctt	120
cccacgcagg cagcagcggg gccggtcaat gaactccact cgtggcttgg ggttgacggt	180
taantgcagg aagaggctga ccacctcgcg gtccaccagg atgcccgaact gtgcgggacc	240
tgcagcgaaa ctctcgatg gtcagagcg ggaagcgaat gangcccagg gccttgccca	300
gaacctccg cctgttctct ggcgtcacct gcagctgctg ccgctnacac tcggcctcgg	360
accagcggac aaacggcggt gaacagccgc acctcacgga tgcccantgt gtcgcgtcc	420
aggaacggcn ccagcgtgtc caggtcaatg tcggtgaanc ctccgcgggt aatggcg	477

<210> 93
 <211> 377
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(377)
 <223> n = A,T,C or G

<400> 93	
gaacggctgg accttgctc gcattgtgct gctggcagga ataccttggc aagcagctcc	60
agtccgagca gccccagacc gctgcgcgcc gaagctaagc ctgcctctgg ccttcccctc	120
cgcctcaatg cagaaccant agtgggagca ctgtgtttag agttaagagt gaacactgtn	180

tgattttact tgggaatttc ctctgttata tagcttttcc caatgcta	ttccaaacaa	240
caacaacaaa ataacatggt tgctgttna gttgtataaa agtangtgat	tctgtatnta	300
aagaaaatat tactgttaca tatactgctt gcaanttctg tatttattgg	tnctctggaa	360
ataaatatat tatta		377

<210> 94
 <211> 495
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(495)
 <223> n = A,T,C or G

<400> 94		
ccctttgagg ggttaggggc cagttcccag tggaagaaac aggccaggag	aantgcgtgc	60
cgagctgang cagatttccc acagtgaccc cagagccctg ggctatagtc	tctgaccctt	120
ccaaggaaaag accaccttct ggggacatgg gctggagggc aggacctaga	ggcaccaagg	180
gaaggcccca ttccggggct gttccccgag gaggaaggga aggggctctg	tgtgcccccc	240
acgaggaana ggccctgant cctgggatca nacaccctt cacgtgtatc	cccacacaaa	300
tgcaagctca ccaaggcccc ctctcagtc cttccctaca ccctgaacgg	ncactggccc	360
accccaccc agancancca cccgccatgg ggaatgttct caaggaatcg	cngggcaacg	420
tgactctng tcccnnaagg ggcagaatc tccaatagan gganngaacc	cttgctnana	480
aaaaaaaana aaaaa		495

<210> 95
 <211> 472
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(472)
 <223> n = A,T,C or G

<400> 95		
ggttacttgg ttctattgcc accacttagt ggatgtcatt tagaaccatt	ttgtctgtc	60
cctctggaag ccttgccgag agcggacttt gtaattgttg gagaataact	gctgaatttt	120
tagctgtttt gagtggatgc gcaccactgc accacaactc aatatgaaa	ctatttnact	180
tatttattat cttgtgaaa gtatacaatg aaaattttgt tcatactgta	tttatcaagt	240
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<212> DNA

<213> Homo sapien

<220>

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<223> n = A,T,C or G

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<210> 98

<211> 461

<212> DNA

<213> Homo sapien

<400> 98

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<211> 171

<212> DNA

<213> Homo sapien

<400> 99

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<212> DNA

<213> Homo sapien

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<211> 405

<212> DNA

<213> Homo sapien

<400> 101

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<213> Homo sapien

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<212> DNA

<213> Homo sapien

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<213> Homo sapien

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<212> DNA

<213> Homo sapien

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<212> DNA

<213> Homo sapien

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<210> 108

<211> 382

<212> PRT

<213> Homo. sapien

<400> 108

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Arg Arg Gly Val Met Glu Lys Leu Gln Leu Gly Pro Glu Ile Leu Gln
85     90     95
Arg Glu Asn Pro Arg Leu Ile Tyr Ala Arg Leu Ser Gly Phe Gly Gln
100    105    110
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115    120    125
Leu Ser Gly Val Leu Ser Lys Ile Gly Arg Ser Gly Glu Asn Pro Tyr
130    135    140
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165    170    175
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Tyr Glu Leu Leu Ile Lys Gly Leu Gly Leu Lys Ser Asp Glu Leu Pro
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 <212> DNA
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aaaaaaaaaa	aaaaaaaaaa	aaaaaaaaaa	aaaaaaaaaa	aaaaaaaaaa	aaaaaaaaaa	3410

<210> 111

<211> 1289

<212> DNA

<213> Homo sapien

<400> 111

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ccatgcagtg	cttcagcttc	attaagacca	tgatgatcct	cttcaatttg	ctcatctttc	180
tgtgtggtgc	agccctggtg	gcagtgggca	tctgggtgtc	aatcgatggg	gcaccccttc	240
tgaagatctt	cgggccactg	tcgtccagtg	ccatgcagtt	tgtaacgtg	ggctacttcc	300
tcattcgacg	cggcgttgtg	gtctttgtc	ttggtttcct	ggcgtgctat	ggtgtaaga	360
ctgagagcaa	gtgtgccctc	gtgacgttct	tcttcactcct	cctcctcatc	ttcattgtg	420
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tgctggtagt	gcctgccatc	aagaagatt	atggttccca	ggaagacttc	actcaagtgt	540
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tagtggatgat	cccagtgtc	tactggggga	tgagagaaag	gcattttata	gcctgggcat	1200
aagtgaatc	agcagagcct	ctgggtggat	gtgtagaagg	cacttcaaaa	tgcataaacc	1260
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<210> 112

<211> 315

<212> PRT

<213> Homo sapien

<400> 112

Met	Val	Phe	Thr	Val	Arg	Leu	Leu	His	Ile	Phe	Thr	Val	Asn	Lys	Gln
1				5				10						15	
Leu	Gly	Pro	Lys	Ile	Val	Ile	Val	Ser	Lys	Met	Met	Lys	Asp	Val	Phe
			20					25					30		
Phe	Phe	Leu	Phe	Phe	Leu	Gly	Val	Trp	Leu	Val	Ala	Tyr	Gly	Val	Ala
		35					40					45			
Thr	Glu	Gly	Leu	Leu	Arg	Pro	Arg	Asp	Ser	Asp	Phe	Pro	Ser	Ile	Leu
	50					55				60					
Arg	Arg	Val	Phe	Tyr	Arg	Pro	Tyr	Leu	Gln	Ile	Phe	Gly	Gln	Ile	Pro
65				70				75						80	
Gln	Glu	Asp	Met	Asp	Val	Ala	Leu	Met	Glu	His	Ser	Asn	Cys	Ser	Ser
			85					90					95		
Glu	Pro	Gly	Phe	Trp	Ala	His	Pro	Pro	Gly	Ala	Gln	Ala	Gly	Thr	Cys
			100				105						110		
Val	Ser	Gln	Tyr	Ala	Asn	Trp	Leu	Val	Val	Leu	Leu	Leu	Val	Ile	Phe
		115					120					125			
Leu	Leu	Val	Ala	Asn	Ile	Leu	Leu	Val	Asn	Leu	Leu	Ile	Ala	Met	Phe
	130					135				140					
Ser	Tyr	Thr	Phe	Gly	Lys	Val	Gln	Gly	Asn	Ser	Asp	Leu	Tyr	Trp	Lys
145				150				155						160	
Ala	Gln	Arg	Tyr	Arg	Leu	Ile	Arg	Glu	Phe	His	Ser	Arg	Pro	Ala	Leu
			165				170						175		
Ala	Pro	Pro	Phe	Ile	Val	Ile	Ser	His	Leu	Arg	Leu	Leu	Leu	Arg	Gln
			180				185						190		
Leu	Cys	Arg	Arg	Pro	Arg	Ser	Pro	Gln	Pro	Ser	Ser	Pro	Ala	Leu	Glu

195	200	205
His Phe Arg Val Tyr Leu Ser Lys Glu Ala Glu Arg Lys Leu Leu Thr		
210	215	220
Trp Glu Ser Val His Lys Glu Asn Phe Leu Leu Ala Arg Ala Arg Asp		
225	230	235
Lys Arg Glu Ser Asp Ser Glu Arg Leu Lys Arg Thr Ser Gln Lys Val		
245	250	255
Asp Leu Ala Leu Lys Gln Leu Gly His Ile Arg Glu Tyr Glu Gln Arg		
260	265	270
Leu Lys Val Leu Glu Arg Glu Val Gln Gln Cys Ser Arg Val Leu Gly		
275	280	285
Trp Val Ala Glu Ala Leu Ser Arg Ser Ala Leu Leu Pro Pro Gly Gly		
290	295	300
Pro Pro Pro Pro Asp Leu Pro Gly Ser Lys Asp		
305	310	315

<210> 113
 <211> 553
 <212> PRT
 <213> Homo sapien

<400> 113

Met Val Gln Arg Leu Trp Val Ser Arg Leu Leu Arg His Arg Lys Ala		
1	5	10
Gln Leu Leu Leu Val Asn Leu Leu Thr Phe Gly Leu Glu Val Cys Leu		
20	25	30
Ala Ala Gly Ile Thr Tyr Val Pro Pro Leu Leu Leu Glu Val Gly Val		
35	40	45
Glu Glu Lys Phe Met Thr Met Val Leu Gly Ile Gly Pro Val Leu Gly		
50	55	60
Leu Val Cys Val Pro Leu Leu Gly Ser Ala Ser Asp His Trp Arg Gly		
65	70	75
Arg Tyr Gly Arg Arg Arg Pro Phe Ile Trp Ala Leu Ser Leu Gly Ile		
85	90	95
Leu Leu Ser Leu Phe Leu Ile Pro Arg Ala Gly Trp Leu Ala Gly Leu		
100	105	110
Leu Cys Pro Asp Pro Arg Pro Leu Glu Leu Ala Leu Leu Ile Leu Gly		
115	120	125
Val Gly Leu Leu Asp Phe Cys Gly Gln Val Cys Phe Thr Pro Leu Glu		
130	135	140
Ala Leu Leu Ser Asp Leu Phe Arg Asp Pro Asp His Cys Arg Gln Ala		
145	150	155
Tyr Ser Val Tyr Ala Phe Met Ile Ser Leu Gly Gly Cys Leu Gly Tyr		
165	170	175
Leu Leu Pro Ala Ile Asp Trp Asp Thr Ser Ala Leu Ala Pro Tyr Leu		
180	185	190
Gly Thr Gln Glu Glu Cys Leu Phe Gly Leu Leu Thr Leu Ile Phe Leu		
195	200	205
Thr Cys Val Ala Ala Thr Leu Leu Val Ala Glu Glu Ala Ala Leu Gly		
210	215	220
Pro Thr Glu Pro Ala Glu Gly Leu Ser Ala Pro Ser Leu Ser Pro His		
225	230	235
Cys Cys Pro Cys Arg Ala Arg Leu Ala Phe Arg Asn Leu Gly Ala Leu		
245	250	255
Leu Pro Arg Leu His Gln Leu Cys Cys Arg Met Pro Arg Thr Leu Arg		
260	265	270
Arg Leu Phe Val Ala Glu Leu Cys Ser Trp Met Ala Leu Met Thr Phe		
275	280	285

Thr Leu Phe Tyr Thr Asp Phe Val Gly Glu Gly Leu Tyr Gln Gly Val
 290 295 300
 Pro Arg Ala Glu Pro Gly Thr Glu Ala Arg Arg His Tyr Asp Glu Gly
 305 310 315 320
 Val Arg Met Gly Ser Leu Gly Leu Phe Leu Gln Cys Ala Ile Ser Leu
 325 330 335
 Val Phe Ser Leu Val Met Asp Arg Leu Val Gln Arg Phe Gly Thr Arg
 340 345 350
 Ala Val Tyr Leu Ala Ser Val Ala Ala Phe Pro Val Ala Ala Gly Ala
 355 360 365
 Thr Cys Leu Ser His Ser Val Ala Val Val Thr Ala Ser Ala Ala Leu
 370 375 380
 Thr Gly Phe Thr Phe Ser Ala Leu Gln Ile Leu Pro Tyr Thr Leu Ala
 385 390 395 400
 Ser Leu Tyr His Arg Glu Lys Gln Val Phe Leu Pro Lys Tyr Arg Gly
 405 410 415
 Asp Thr Gly Gly Ala Ser Ser Glu Asp Ser Leu Met Thr Ser Phe Leu
 420 425 430
 Pro Gly Pro Lys Pro Gly Ala Pro Phe Pro Asn Gly His Val Gly Ala
 435 440 445
 Gly Gly Ser Gly Leu Leu Pro Pro Pro Ala Leu Cys Gly Ala Ser
 450 455 460
 Ala Cys Asp Val Ser Val Arg Val Val Val Gly Glu Pro Thr Glu Ala
 465 470 475 480
 Arg Val Val Pro Gly Arg Gly Ile Cys Leu Asp Leu Ala Ile Leu Asp
 485 490 495
 Ser Ala Phe Leu Leu Ser Gln Val Ala Pro Ser Leu Phe Met Gly Ser
 500 505 510
 Ile Val Gln Leu Ser Gln Ser Val Thr Ala Tyr Met Val Ser Ala Ala
 515 520 525
 Gly Leu Gly Leu Val Ala Ile Tyr Phe Ala Thr Gln Val Val Phe Asp
 530 535 540
 Lys Ser Asp Leu Ala Lys Tyr Ser Ala
 545 550

<210> 114

<211> 241

<212> PRT

<213> Homo sapien

<400> 114

Met Gln Cys Phe Ser Phe Ile Lys Thr Met Met Ile Leu Phe Asn Leu
 1 5 10 15
 Leu Ile Phe Leu Cys Gly Ala Ala Leu Leu Ala Val Gly Ile Trp Val
 20 25 30
 Ser Ile Asp Gly Ala Ser Phe Leu Lys Ile Phe Gly Pro Leu Ser Ser
 35 40 45
 Ser Ala Met Gln Phe Val Asn Val Gly Tyr Phe Leu Ile Ala Ala Gly
 50 55 60
 Val Val Val Phe Ala Leu Gly Phe Leu Gly Cys Tyr Gly Ala Lys Thr
 65 70 75 80
 Glu Ser Lys Cys Ala Leu Val Thr Phe Phe Phe Ile Leu Leu Leu Ile
 85 90 95
 Phe Ile Ala Glu Val Ala Ala Ala Val Val Ala Leu Val Tyr Thr Thr
 100 105 110
 Met Ala Glu His Phe Leu Thr Leu Leu Val Val Pro Ala Ile Lys Lys
 115 120 125
 Asp Tyr Gly Ser Gln Glu Asp Phe Thr Gln Val Trp Asn Thr Thr Met

130		135		140
Lys Gly Leu Lys Cys Cys Gly Phe Thr Asn Tyr Thr Asp Phe Glu Asp				
145		150		155
Ser Pro Tyr Phe Lys Glu Asn Ser Ala Phe Pro Pro Phe Cys Cys Asn				
	165		170	175
Asp Asn Val Thr Asn Thr Ala Asn Glu Thr Cys Thr Lys Gln Lys Ala				
	180		185	190
His Asp Gln Lys Val Glu Gly Cys Phe Asn Gln Leu Leu Tyr Asp Ile				
	195		200	205
Arg Thr Asn Ala Val Thr Val Gly Gly Val Ala Ala Gly Ile Gly Gly				
	210		215	220
Leu Glu Leu Ala Ala Met Ile Val Ser Met Tyr Leu Tyr Cys Asn Leu				
225		230		235
Gln				240

<210> 115
 <211> 366
 <212> DNA
 <213> Homo sapien

<400> 115
 gctctttctc tcccctctc tgaatttaaat tctttcaact tgcaatttgc aaggattaca 60
 catttcactg tgatgtatat tgtgttgcaa aaaaaaaaaa gtgtctttgt ttaaaattac 120
 ttggtttgtg aatccatctt gctttttccc cattggaact agtcattaac ccatctctga 180
 actggtagaa aaacatctga agagctagtc tatcagcatc tgacaggtga attggatggt 240
 tctcagaacc atttcaccca gacagcctgt ttctatcctg ttttaataaat tagtttgggt 300
 tctctacatg cataacaaac cctgctccaa tctgtcacat aaaagtctgt gacttgaagt 360
 ttagtc 366

<210> 116
 <211> 282
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(282)
 <223> n = A,T,C or G

<400> 116
 acaaagatga accatttcct atattatagc aaaattaaaa tctaccgta ttctaattatt 60
 gagaaatgag atnaaacaca atnttataaa gtctacttag agaagatcaa gtgacctcaa 120
 agactttact attttcatat tttaagacac atgatttatc ctatttttagt aacctgggtc 180
 atacgttaaa caaaggataa tgtgaacagc agagaggatt tgttggcaga aaatctatgt 240
 tcaatctnga actatctana tcacagacat ttctattcct tt 282

<210> 117
 <211> 305
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(305)
 <223> n = A,T,C or G

<400> 117

```

acacatgtcg cttcactgcc ttcttagatg cttctggtca acatanagga acagggacca      60
tatttatcct ccttcctgaa acaattgcaa aataanacaa aatatatgaa acaattgcaa      120
aataaggcaa aatatatgaa acaacaggtc tcgagatatt ggaaatcagt caatgaagga      180
tactgatccc tgatcactgt cctaatgcag gatgtgggaa acagatgagg tcacctctgt      240
gactgcccca gcttactgcc tgtagagagt ttctangctg cagttcagac agggagaaat      300
tggtt                                           305

```

<210> 118

<211> 71

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (71)

<223> n = A,T,C or G

<400> 118

```

accaaggtgt ntgaatctct gacgtgggga tctctgattc ccgcacaatc tgagtggaaa      60
aantcctggg t                                           71

```

<210> 119

<211> 212

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (212)

<223> n = A,T,C or G

<400> 119

```

actccggttg gtgtcagcag cacgtggcat tgaacatngc aatgtggagc ccaaaccaca      60
gaaaatgggg tgaaattggc caactttcta tnaacttatg ttggcaantt tgccaccaac      120
agtaagctgg cccttctaataaaaagaaaat tgaaaggttt ctcactaanc ggaattaant      180
aatggantca aganactccc aggctcagc gt                                           212

```

<210> 120

<211> 90

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (90)

<223> n = A,T,C or G

<400> 120

```

actcgttgca natcaggggc cccccagagt caccgttgca ggagtccttc tggctcttgcc      60
ctccgccggc gcagaacatg ctggggtggt                                           90

```

<210> 121

<211> 218

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(218)

<223> n = A,T,C or G

<400> 121

tgtancgtga anacgacaga nagggttgtc aaaaatggag aanccttgaa gtcattttga	60
gaataagatt tgctaaaaga tttggggcta aaacatgggt attgggagac atttctgaag	120
atatncangt aaattangga atgaattcat ggttcttttg ggaattcctt tacgatngcc	180
agcatanact tcatgtgggg atancagcta cccttgta	218

<210> 122

<211> 171

<212> DNA

<213> Homo sapien

<400> 122

taggggtgta tgcaactgta aggacaaaaa ttgagactca actggcttaa ccaataaagg	60
catttggttag ctcatggaac aggaagtcgg atggtggggc atcttcagtg ctgcatgagt	120
caccaccccg gcgggggtcat ctgtgccaca ggtccctgtt gacagtgcgg t	171

<210> 123

<211> 76

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(76)

<223> n = A,T,C or G

<400> 123

tgtagcgtga agacnacaga atggtgtgtg ctgtgctatc caggaacaca tttattatca	60
ttatcaanta ttgtgt	76

<210> 124

<211> 131

<212> DNA

<213> Homo sapien

<400> 124

acctttcccc aaggccaatg tctgtgtgac taactggccg gctgcaggac agctgcaatt	60
caatgtgctg ggtcatatgg aggggaggag actctaaaat agccaatttt attctcttgg	120
ttaagatttg t	131

<210> 125

<211> 432

<212> DNA

<213> Homo sapien

<400> 125

acttttatcta ctggctatga aatagatggt ggaaaattgc gttaccaact ataccactgg	60
cttgaaaaag aggtgatagc tcttcagagg acttgtgact tttgctcaga tgctgaagaa	120
ctacagtctg catttggcag aaatgaagat gaatttgat taaatgagga tgctgaagat	180
ttgcctcacc aaacaaaagt gaaacaactg agagaaaatt ttcaggaaaa aagacagtgg	240
ctcttgaagt atcagtcact tttgagaatg tttcttagtt actgcatact tcatggatcc	300
catggtgggg gtcttgcac tgtaagaatg gaattgattt tgcttttgca agaattctcag	360
caggaaacat cagaaccact attttctagc cctctgtcag agcaaacctc agtgcctctc	420
ctctttgctt gt	432

<210> 126
 <211> 112
 <212> DNA
 <213> Homo sapien

<400> 126
 acacaacttg aatagtaaaa tagaaactga gctgaaatth ctaattcact ttctaaccat 60
 agtaagaatg atatttcccc ccagggatca ccaaatatth ataaaaatth gt 112

<210> 127
 <211> 54
 <212> DNA
 <213> Homo sapien

<400> 127
 accacgaaac cacaacaag atggaagcat caatccactt gccaaacaca gcag 54

<210> 128
 <211> 323
 <212> DNA
 <213> Homo sapien

<400> 128
 acctcattag taattgtttt gttgtttcat ttttttctaa tgtctcccct ctaccagctc 60
 acctgagata acagaatgaa aatggaagga cagccagatt tctcctttgc tctctgctca 120
 ttctctctga agtctaggtt acccattttg gggaccatt ataggcaata aacacagttc 180
 ccaaagcatt tggacagttt cttgttgtgt tttagaatgg ttttcctttt tcttagcctt 240
 ttctgcaaaa aggtcactc agtcccttgc ttgctcagtg gactgggctc cccagggcct 300
 aggtgcctt cttttccatg tcc 323

<210> 129
 <211> 192
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(192)
 <223> n = A,T,C or G

<400> 129
 acatacatgt gtgtatattt ttaaataatca cttttgtatc actctgactt tttagcatac 60
 tgaaaacaca ctaacataat ttntgtgaac catgatcaga tacaacccaa atcattcatc 120
 tagcacattc atctgtgata naaagatagg tgagtttcat ttctttcacg ttggccaatg 180
 gataaacaaa gt 192

<210> 130
 <211> 362
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(362)
 <223> n = A,T,C or G

<400> 130
 ccctttttta tgggaatgagt agactgtatg tttgaanatt tanccacaac ctctttgaca 60

tataatgacg	caacaaaaag	gtgctgttta	gtcctatggt	tcagtttatg	cccctgacaa	120
gtttccattg	tgttttgceg	atcttctggc	taatcgtggt	atcctccatg	ttattagtaa	180
ttctgtatc	catttttgta	acgcctggta	gatgtaacct	gctangagge	taactttata	240
cttattttaa	agctcttatt	ttgtggatcat	taaaatggca	atztatgtgc	agcactttat	300
tgacgcagga	agcacgtgtg	ggttggttgt	aaagctcttt	gctaattctta	aaaagtaatg	360
gg						362

<210> 131
 <211> 332
 <212> DNA
 <213> Homo sapien

 <220>
 <221> misc_feature
 <222> (1)...(332)
 <223> n = A,T,C or G

<400> 131						
ctttttgaaa	gatcgtgtcc	actcctgtgg	acatcttgtt	ttaatggagt	ttcccatgca	60
gtangactgg	tatgggttga	gctgtccaga	taaaaacatt	tgaagagctc	caaaatgaga	120
gttctcccag	gttcgcctcg	ctgctccaag	tctcagcagc	agcctctttt	aggaggcatc	180
ttctgaacta	gattaaggca	gcttgtaaat	ctgatgtgat	ttgggtttatt	atccaactaa	240
cttccatctg	ttatcactgg	agaaagccca	gactccccan	gacnggtacg	gatttgtggc	300
atanaaggat	tgggtgaagc	tggcgttgtg	gt			332

<210> 132
 <211> 322
 <212> DNA
 <213> Homo sapien

 <220>
 <221> misc_feature
 <222> (1)...(322)
 <223> n = A,T,C or G

<400> 132						
acttttgcca	ttttgtatat	ataaacaatc	ttgggacatt	ctcctgaaaa	ctaggtgtcc	60
agtggctaag	agaactcgat	ttcaagcaat	tctgaaagga	aaaccagcat	gacacagaat	120
ctcaaatcc	caaacagggg	ctctgtggga	aaaatgaggg	aggacctttg	tatctcgggt	180
tttagcaagt	taaaatgaan	atgacaggaa	aggettattt	atcaacaaag	agaagagttg	240
ggatgcttct	aaaaaaaaact	ttggtagaga	aaataggaat	gctnaatcct	aggggaagcct	300
gtaacaatct	acaattggtc	ca				322

<210> 133
 <211> 278
 <212> DNA
 <213> Homo sapien

 <220>
 <221> misc_feature
 <222> (1)...(278)
 <223> n = A,T,C or G

<400> 133						
acaagccttc	acaagtttaa	ctaaattggg	attaatcttt	ctgtanttat	ctgcataatt	60
cttggttttc	tttccatctg	gctcctgggt	tgacaatttg	tggaaacaac	tctattgcta	120
ctatttataa	aaaatcacaa	atctttccct	ttaagctatg	ttnaattcaa	actattcctg	180
ctattcctgt	tttgtcaaag	aaatttatatt	tttcaaaata	tgtntatttg	tttgatgggt	240

cccacgaaac actaataaaa accacagaga ccagcctg

278

<210> 134

<211> 121

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(121)

<223> n = A,T,C or G

<400> 134

gtttanaaaa	cttgtttagc	tccatagagg	aaagaatggt	aaactttgta	ttttaaaaca	60
tgattctctg	aggttaaact	tggttttcaa	atgttatttt	tacttgatt	ttgcttttgg	120
t						121

<210> 135

<211> 350

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(350)

<223> n = A,T,C or G

<400> 135

acttanaacc	atgcctagca	catcagaatc	cctcaaagaa	catcagtata	atcctataacc	60
atancaagtg	gtgactgggt	aagcgtgcga	caaagggtcag	ctggcacatt	acttggtgtc	120
aaacttgata	cttttgttct	aagtaggaac	tagtatacag	tncctaggan	tggtactcca	180
gggtgcccc	caactcctgc	agccgctcct	ctgtgccagn	ccctgnaagg	aaactttcgt	240
ccacctcaat	caagccctgg	gccatgctac	ctgcaattgg	ctgaacaaac	gtttgctgag	300
ttcccaagga	tgcaaagcct	ggtgctcaac	tcttggggcg	tcaactcagt		350

<210> 136

<211> 399

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(399)

<223> n = A,T,C or G

<400> 136

tgtaccgtga	agacgacaga	agttgcatgg	cagggacagg	gcagggccga	ggccagggtt	60
gctgtgattg	tatccgaata	ntcctcgtga	gaaaagataa	tgagatgacg	tgagcagcct	120
gcagacttgt	gtctgccttc	aanaagccag	acaggaaggc	cctgcctgcc	ttggctctga	180
cctggcgccc	agccagccag	ccacaggtgg	gcttcttcct	tttgtggtga	caacnccaag	240
aaaactgcag	aggcccagg	tcaggtgtna	gtgggtangt	gaccataaaa	caccaggtgc	300
tcccaggaac	ccgggcaaag	gccatcccca	cctacagcca	gcatgcccac	tggcgtgatg	360
ggtgcagang	gatgaagcag	ccagntgttc	tgctgtggt			399

<210> 137

<211> 165

<212> DNA

<213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(165)
 <223> n = A,T,C or G

<400> 137
 actggtgtgg tnggggggtga tgctggtggt anaagttgan gtgacttcan gatggtgtgt 60
 ggaggaagtg tgtgaacgta gggatgtaga ngttttggcc gtgctaaatg agcttcggga 120
 ttggctggtc ccactggtgg tcaactgtcat tgggtggggt cctgt 165

<210> 138
 <211> 338
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(338)
 <223> n = A,T,C or G

<400> 138
 actcactgga atgccacatt cacaacagaa tcagaggtct gtgaaaacat taatggctcc 60
 ttaacttctc cagtaagaat cagggacttg aaatggaaac gttaacagcc acatgcccaa 120
 tgctgggcag tctcccatgc cttccacagt gaaagggctt gagaaaaatc acatccaatg 180
 tcatgtgttt ccagccacac caaaaggtgc ttgggggtgga gggctggggg catananggt 240
 cangcctcag gaagcctcaa gtccattca gctttgccac tgtacattcc ccatntttaa 300
 aaaaactgat gccttttttt tttttttttg taaaattc 338

<210> 139
 <211> 382
 <212> DNA
 <213> Homo sapien

<400> 139
 gggaatcttg gtttttggca tctggtttgc ctatagccga ggccactttg acagaacaaa 60
 gaaagggact tcgagtaaga aggtgattta cagccagcct agtgcccgaa gtgaaggaga 120
 attcaaacag acctcgatc tctggtgtg agcctggtcg gctcacgcc tatcatctgc 180
 atttgctta ctcaggtgct accggactct ggccctgat gtctgtagtt tcacaggatg 240
 ccttatttgt cttctacacc ccacagggcc ccctacttct tcggatgtgt ttttaataat 300
 gtcagctatg tgcccatcc tcttcatgc cctccctccc tttcctacca ctgctgagtg 360
 gcctggaact tgtttaaagt gt 382

<210> 140
 <211> 200
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(200)
 <223> n = A,T,C or G

<400> 140
 accaaanctt ctttctgttg tgttngattt tactataggg gtttngcttn ttctaaanat 60
 acttttcatt taacancttt tgttaagtgt caggtgcac tttgctccat anaattattg 120
 ttttcacatt tcaacttgta tgtgtttgtc tcttanagca ttggtgaaat cacatatttt 180
 atattcagca taaaggagaa 200

<210> 141
 <211> 335
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1) ... (335)
 <223> n = A,T,C or G

<400> 141
 actttatattt caaaacactc atatgttgca aaaaacacat agaaaaataa agtttggtgg 60
 ggggtgctgac taaacttcaa gtcacagact tttatgtgac agattggagc agggtttggt 120
 atgcatgtag agaaccctaa ctaatttatt aaacaggata gaaacaggct gtctgggtga 180
 aatgggtctg agaaccatcc aattcacctg tcagatgctg atanactagc tcttcagatg 240
 tttttctacc agttcagaga tnggttaatg actanttcca atggggaaaa agcaagatgg 300
 attcacaac caagtaattt taaacaaga cactt 335

<210> 142
 <211> 459
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1) ... (459)
 <223> n = A,T,C or G

<400> 142
 accagggttaa tattgccaca tatatccttt ccaattgctg gctaaacaga cgtgtattta 60
 ggggtgtttaa aagacaaccc agcttaatat caagagaaat tgtgacctt catggagtat 120
 ctgatggaga aaacactgag ttttgacaaa tcttatttta ttcagatagc agtctgatca 180
 cacatgggtcc aacaacactc aaataataaa tcaaatatna tcagatgtta aagattggtc 240
 ttcaaacatc atagccaatg atgcccogct tgcctataat ctctccgaca taaaaccaca 300
 tcaacacctc agtggccacc aaaccattca gcacagcttc cttaactgtg agctgtttga 360
 agctaccagt ctgagcacta ttgactatnt ttttcangct ctgaatagct ctagggatct 420
 cagcanggggt gggaggaacc agctcaacct tggcgtant 459

<210> 143
 <211> 140
 <212> DNA
 <213> Homo sapien

<400> 143
 acatttcctt ccaccaagtc aggactcctg gcttctgtgg gagttcttat cacctgaggg 60
 aaatccaaac agtctctcct agaaaggaat agtgtcacca accccaccca tctccctgag 120
 accatccgac ttcctgtgt 140

<210> 144
 <211> 164
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1) ... (164)
 <223> n = A,T,C or G

<400> 144
 acttcagtaa caacatacaa taacaacatt aagtgtatat tgccatcttt gtcattttct 60
 atctatacca ctctcccttc tgaaaacaan aatcactanc caatcactta tacaaatttg 120
 aggcaattaa tccatatttg ttttcaataa ggaaaaaaag atgt 164

<210> 145

<211> 303

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(303)

<223> n = A,T,C or G

<400> 145
 acgtagacca tccaactttg tatttgtaat ggcaaacatc cagnagcaat tcctaaacaa 60
 actggagggt atttataccc aattatccca ttcattaaca tgccctcttc ctcaggctat 120
 gcaggacagc tatcataagt cggcccaggc atccagatac taccatttgg ataaacttca 180
 gtaggggagt ccatccaagt gacaggtcta atcaaaggag gaaatggaac ataagcccag 240
 tagtaaaatn ttgcttagct gaaacagcca caaaagactt accgccgtgg tgattaccat 300
 caa 360

<210> 146

<211> 327

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(327)

<223> n = A,T,C or G

<400> 146
 actgcagctc aattagaagt ggtctctgac tttcatcanc ttctccctgg gctccatgac 60
 actggcctgg agtgactcat tgctctgggt gggtgagaga gctcctttgc caacaggcct 120
 ccaagtcagg gctgggattt gtttccttcc cacattctag caacaatatg ctggccactt 180
 cctgaacagg gaggggtgga ggagccagca tggaacaagc tgccactttc taaagtagcc 240
 agacttgccc ctgggcctgt cacacctact gatgaccttc tgtgcctgca ggatggaatg 300
 taggggtgag ctgtgtgact ctatggt 360

<210> 147

<211> 173

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(173)

<223> n = A,T,C or G

<400> 147
 acattgtttt tttgagataa agcattgana gagctctcct taacgtgaca caatggaagg 60
 actggaacac ataccacat ctttgttctg agggataatt ttctgataaa gtcttgctgt 120
 atattcaagc acatatgtta tatattatc agttccatgt ttatagccta gtt 173

<210> 148

<211> 477
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1) ... (477)
 <223> n = A,T,C or G

<400> 148
 acaaccactt tatctcatcg aatttttaac ccaaactcac tcactgtgcc tttctatcct 60
 atgggatata ttatttgatg ctccatttca tcacacatat atgaataata cactcatact 120
 gccctactac ctgctgcaat aatcacattc ccttcctgtc ctgaccctga agccattggg 180
 gtggctcctag tggccatcag tccangcctg caccttgagc ccttgagctc cattgtcac 240
 nccancccac ctcaccgacc ccattcctctt acacagctac ctccttgctc tctaacccca 300
 tagattatnt ccaaattcag tcaattaagt tactattaac actctacccg acatgtccag 360
 caccactggg aagccttctc cagccaacac acacacacac acacacatat 420
 ccaggcacag gctacctcat cttcacaatc acccctttaa ttaccatgct atgggtgg 477

<210> 149
 <211> 207
 <212> DNA
 <213> Homo sapien

<400> 149
 acagttgtat tataatatca agaaataaac ttgcaatgag agcatttaag agggaagaac 60
 taacgtatnt tagagagcca aggaagggtt ctgtggggag tgggatgtaa ggtggggcct 120
 gatgataaat aagagtcagc caggtaagtg ggtggtgtgg tatgggcaca gtgaagaaca 180
 ttccaggcag agggaacagc agtgaac 207

<210> 150
 <211> 111
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1) ... (111)
 <223> n = A,T,C or G

<400> 150
 accttgatnt cattgctgct ctgatggaaa cccaactatc taatttagct aaaacatggg 60
 cacttaaatg tggtcagtgt ttggacttgt taactantgg catctttggg t 111

<210> 151
 <211> 196
 <212> DNA
 <213> Homo sapien

<400> 151
 agcgcgccag gtcattatga acattccaga tacctatcat tactcgatgc tgttgataac 60
 agcaagatgg ctttgaactc agggtcacca ccagctattg gaccttacta tgaaaaccat 120
 ggataccaac cggaaaaccc ctatcccgca cagcccactg tgggtcccccac tgtctacgag 180
 gtgcatccgg ctcagt 196

<210> 152
 <211> 132
 <212> DNA

<213> Homo sapien

<400> 152

acagcacttt cacatgtaag aagggagaaa ttcctaaatg taggagaaag ataacagAAC	60
cttccccttt tcatctagt gtggaaacct gatgctttat gttgacagga atagaaccag	120
gagggagttt gt	132

<210> 153

<211> 285

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)... (285)

<223> n = A,T,C or G

<400> 153

acaanacca nganaggcca ctggccgtgg tgtcatggcc tccaaacatg aaagtgtcag	60
cttctgctct tatgtcctca tctgacaact ctttaccatt tttatcctcg ctgagcagga	120
gcacatcaat aaagtccaaa gtcttggaact tggccttggc ttggaggaag tcatcaaac	180
cctggctagt gaggggtgcgg cgccgctcct ggatgacggc atctgtgaag tcgtgcacca	240
gtctgcaggc cctgtggaag cgccgtccac acggagtnag gaatt	285

<210> 154

<211> 333

<212> DNA

<213> Homo sapien

<400> 154

accacagtcc tgttgggcca gggcttcatg accctttctg tgaaaagcca tattatcacc	60
accccaaatt tttccttaaa tatctttaac tgaaggggtc agcctcttga ctgcaaagac	120
cctaagccgg ttacacagct aactcccact ggccctgatt tgtgaaattg ctgctgcctg	180
attggcacag gactcgaagg ttttcagctc ccctcctcgg tggaaacgaga ctctgatttg	240
agtttcacaa attctcgggc cacctcgtca ttgctcctct gaaataaaat ccggagaatg	300
gtcaggcctg tctcatccat atggatcttc cgg	333

<210> 155

<211> 308

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)... (308)

<223> n = A,T,C or G

<400> 155

actggaaata ataaaacca catcacagtg ttgtgtcaaa gatcatcagg gcatggatgg	60
gaaagtgcct tgggaactgt aaagtgccta acacatgatc gatgattttt gttataatat	120
ttgaatcacg gtgcatacaa actctcctgc ctgctcctcc tgggccccag cccagcccc	180
atcacagctc actgctctgt tcatccaggc ccagcatgta gtggctgatt cttcttggct	240
gcttttagcc tccanaagtt tctctgaagc caaccaaacc tctangtgta aggcattgctg	300
gccctggg	308

<210> 156

<211> 295

<212> DNA

<213> Homo sapien

<400> 156

accttgctcg	gtgcttgga	catattagga	actcaaaata	tgagatgata	acagtgccta	60
ttattgatta	ctgagagaac	tgtagacat	ttagttgaag	atcttctaca	caggaactga	120
gaataggaga	ttatgtttgg	ccctcatatt	ctctcctatc	ctccttgect	cattctatgt	180
ctaatatatt	ctcaatcaaa	taaggttage	ataatcagga	aatcgaccaa	ataccaatat	240
aaaaccagat	gtctatcctt	aagattttca	aatagaaaac	aaattaacag	actat	295

<210> 157

<211> 126

<212> DNA

<213> Homo sapien

<400> 157

acaagtttaa	atagtgctgt	cactgtgcat	gtgctgaaat	gtgaaatcca	ccacatttct	60
gaagagcaaa	acaaattctg	tcatgtaatc	tctatcttgg	gtcgtgggta	tatctgtccc	120
cttagt						126

<210> 158

<211> 442

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (442)

<223> n = A,T,C or G

<400> 158

accactgggt	cttgaaaaca	cccatcctta	atacgatgat	ttttctgtcg	tgtgaaaatg	60
aanccagcag	gctgcccta	gtcagtcctt	ccttcagag	aaaaagagat	ttgagaaagt	120
gcctgggtaa	ttcaccatta	atttcctccc	ccaaactctc	tgagtcttcc	cttaatat	180
ctggtggttc	tgaccaaaagc	aggatcatgg	ttgttgagca	tttgggatcc	cagtgaagta	240
natgtttgta	gccttgcata	cttagccctt	cccacgcaca	aacggagtgg	cagagtgggtg	300
ccaaccctgt	tttcccagtc	cacgtagaca	gattcacagt	gcggaattct	ggaagctgga	360
nacagacggg	ctctttgcag	agccgggact	ctgagangga	catgagggcc	tctgcctctg	420
tgttcattct	ctgatgtcct	gt				442

<210> 159

<211> 498

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (498)

<223> n = A,T,C or G

<400> 159

acttcagggt	aacgtgtgtg	tttccgttga	gcctgaactg	atgggtgacg	ttgtaggttc	60
tccaacaaga	actgaggttg	cagagcgggt	agggagaggt	gctgttccag	ttgcacctgg	120
gctgctgtgg	actgtgtgtg	attcctcact	acggcccaag	gttgtggaac	tggcanaaag	180
gtgtgtgtgt	gganttgagc	tcgggcggct	gtggtaggtt	gtgggtctct	caacaggggc	240
tgctgtgggtg	ccgggagtg	aangtgttgt	gtcacttgag	cttggccagc	tctggaaagt	300
antanattct	tcctgaaggc	cagcgttgt	ggagctggca	ngggtcantg	ttgtgtgtaa	360
cgaaccagtg	ctgctgtggg	tgggtgtana	tcctccacaa	agcctgaagt	tatggtgtcn	420
tcaggtana	atgtgtgttc	agtgccctg	ggcngctgtg	gaaggttgta	nattgtcacc	480

aagggaataa gctgtggt

498

<210> 160

<211> 380

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(380)

<223> n = A,T,C or G

<400> 160

acctgcatcc agcttcctcg ccaaactcac aaggagacat caacctctag acagggaaac	60
agcttcagga tacttccagg agacagagcc accagcagca aaacaaatat tcccatgcct	120
ggagcatggc atagaggaag ctganaaatg tggggtctga ggaagccatt tgagtctggc	180
cactagacat ctcatcagcc acttgtgtga agagatgccc catgacccca gatgcctctc	240
ccacccttac ctccatctca cacacttgag ctttccactc tgtataattc taacatcctg	300
gagaaaaatg gcagtttgac cgaacctgtt cacaacggta gaggctgatt tctaacgaaa	360
ctttagaat gaagcctgga	380

<210> 161

<211> 114

<212> DNA

<213> Homo sapien

<400> 161

actccacatc cctctgagc aggcggttgt cgttcaaggt gtatttggcc ttgcctgtca	60
cactgtccac tggcccctta tccacttggt gcttaatccc tcgaaagagc atgt	114

<210> 162

<211> 177

<212> DNA

<213> Homo sapien

<400> 162

actttctgaa tcgaatcaaa tgatacttag tgtagtttta atatcctcat atatatcaaa	60
gttttactac tctgataatt ttgtaaacca ggtaaccaga acatccagtc atacagcttt	120
tggtgatata taacttgga ataaccagc ctggtgatac ataaaactac tcactgt	177

<210> 163

<211> 137

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(137)

<223> n = A,T,C or G

<400> 163

catttataca gacaggcgtg aagacattca cgacaaaaac gcgaaattct atcccgtgac	60
canagaaggc agctacggct actcctacat cctggcgtgg gtggccttcg cctgcacctt	120
catcagcggc atgatgt	137

<210> 164

<211> 469

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(469)

<223> n = A,T,C or G

<400> 164

cttatcacaa tgaatgttct cctgggcagc gttgtgatct ttgccacctt cgtgacttta	60
tgcaatgcat catgctatct cacaactaat gagggagttc caggagattc aaccaggaaa	120
tgcatggatc tcaaaggaaa caaacaccca ataaactcgg agtggcagac tgacaactgt	180
gagacatgca cttgtctacga aacagaaatt tcatgttgca cccttgtttc tacacctgtg	240
ggttatgaca aagacaactg ccaaagaatc ttcaagaagg aggactgcaa gtatatcgtg	300
gtggagaaga aggacccaaa aaagacctgt tctgtcagtg aatggataat ctaatgtgct	360
tctagtaggc acagggtccc caggccaggc ctcattctcc tctggcctct aatagtcaat	420
gattgtgtag ccatgcctat cagtaaaaag atntttgagc aaacacttt	469

<210> 165

<211> 195

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(195)

<223> n = A,T,C or G

<400> 165

acagtttttt atanatctg acattgccgg cacttggtgt cagtttcata aagctgggtg	60
atccgctgtc atccactatt ccttggttag agtaaaaatt attcttatag cccatgtccc	120
tgcaggccgc ccgcccgtag ttctcgttcc agtcgtcttg gcacacaggg tgccaggact	180
tcctctgaga tgagt	195

<210> 166

<211> 383

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(383)

<223> n = A,T,C or G

<400> 166

acatcttagt agtgtggcac atcagggggc catcagggtc acagtcactc atagcctcgc	60
cgaggctcga gtccacacca ccggtgtagg tgtgtcfaat cttgggcttg gcgcccacct	120
ttggagaagg gatatgtgtc acacacatgt ccacaaagcc tgtgaactcg ccaaagaatt	180
tttgacagcc agcctgagca aggggcggat gttcagcttc agtcctcctc tcgtcagggtg	240
gatgcccaacc tcgtctangg tccgtgggaa gctgggtgtc acntcaccta caacctgggc	300
gangatctta taaagaggct ccnagataaa ctccacgaaa cttctctggg agctgctagt	360
nggggccttt ttggtgaact ttc	383

<210> 167

<211> 247

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(247)

<223> n = A,T,C or G

<400> 167

acagagccag accttggcca taaatgaanc agagattaag actaaacccc aagtcganat	60
tgagagcagaa actggagcaa gaagtgggcc tggggctgaa gtagagacca aggccactgc	120
tatanccata cacagagcca actctcaggc caaggcnatg gttggggcag anccagagac	180
tcaatctgan tccaaagtgg tggctggaac actggtcatg acanaggcag tgactctgac	240
tgangtc	247

<210> 168

<211> 273

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(273)

<223> n = A,T,C or G

<400> 168

acttctaagt tttctagaag tggaaggatt gtantcatcc tgaaaatggg tttacttcaa	60
aatccctcan ccttgttctt cacnactgtc tatactgana gtgtcatgtt tccacaaagg	120
gctgacacct gagcctgnat tttactcat ccctgagaag ccctttccag taggggtggc	180
aattcccaac ttccttgcca caagcttccc aggctttctc ccctggaaaa ctccagcttg	240
agtcccatgat acatcatgg gctgccttg gca	273

<210> 169

<211> 431

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(431)

<223> n = A,T,C or G

<400> 169

acagccttgg cttcccaaaa ctccacagtc tcagtgcaga aagatcatct tccagcagtc	60
agctcagacc aggtgcaaag gatgtgacat caacagtttc tggtttcaga acaggttcta	120
ctactgtcaa atgaccccc atacttctc aaaggctgtg gtaagttttg cacaggtgag	180
ggcagcagaa agggggtant tactgatgga caccatcttc tctgtatact ccacactgac	240
cttgccatgg gcaaaggccc ctaccacaaa aacaatagga tcaactgctgg gcaccagctc	300
acgcacatca ctgacaaccg ggatggaaaa agaantgcca actttcatac atccaactgg	360
aaagtgatct gatactggat tcttaattac cttcaaaagc ttctgggggc catcagctgc	420
tcgaacactg a	431

<210> 170

<211> 266

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(266)

<223> n = A,T,C or G

```

<400> 170
acctgtgggc tgggctgtta tgctgtgcc ggctgctgaa agggagtcca gaggtggagc      60
tcaaggagct ctgcaggcat ttgccaanc ctctccanag canagggagc aacctacact      120
ccccgctaga aagacaccag attggagtcc tgggaggggg agttgggggtg ggcatttgat      180
gtatacttgt cacctgaatg aangagccag agaggaanga gacgaanatg anattggcct      240
tcaaagctag gggctctggca ggtgga                                     266

```

```

<210> 171
<211> 1248
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(1248)
<223> n = A,T,C or G

```

```

<400> 171
ggcagccaaa tcataaacgg cgaggactgc agcccgcaact cgcagccctg gcaggcggca      60
ctggtcatgg aaaacgaatt gttctgctcg ggctgctgga tgcattccga gtgggtgctg      120
tcagccgcac actgtttcca gaagtgaagt gagagctcct acaccatcgg gctgggcctg      180
cacagtcttg aggcggacca agagccaggg agccagatgg tggaggccag cctctccgta      240
cggcacccag agtacaacag acccttgctc gctaacgacc tcatgctcat caagttggac      300
gaatccgtgt ccgagtctga caccatccgg agcatcagca ttgcttcgca gtgccctacc      360
gcggggaaact cttgcctcgt ttctggctgg ggtctgctgg cgaacggcag aatgcctacc      420
gtgctgcagt gcgtgaacgt gtcggtgggtg tctgaggagg tctgcagtaa gctctatgac      480
ccgctgtacc accccagcat gttctgcgcc ggcgaggagg aagaccagaa ggactcctgc      540
aacggtgact ctggggggcc cctgatctgc aacgggtact tgcagggcct tgtgtctttc      600
ggaaaagccc cgtgtggcca agttggcgtg ccaggtgtct acaccaacct ctgcaaattc      660
actgagtggg tagagaaaac cgtccaggcc agttaactct ggggactggg aacctatgaa      720
attgaccccc aaatacatcc tgcggaagga attcaggaat atctgttccc agccccctct      780
ccctcaggcc caggagtcca ggccccagc ccctcctccc tcaaaccaag ggtacagatc      840
cccagccct cctccctcag acccaggagt ccagaccccc cagccctccc tccctcagac      900
ccaggagtcc agccccctct ccctcagacc caggagtcca gacccccag cccctcctcc      960
ctcagaccca ggggtccagg cccccaaccc ctctcctccc agactcagag gtccaagccc      1020
ccaaccntc attcccaga ccagaggtc caggtccag cccctcntcc ctcagaccca      1080
gcggtccaat gccacctaga cntccctgt acacagtgcc cccttggtgg acgttgaccc      1140
aaccttacca gttggttttt catttttngt ccctttcccc tagatccaga aataaagttt      1200
aagagaagng caaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa      1248

```

```

<210> 172
<211> 159
<212> PRT
<213> Homo sapien

```

```

<220>
<221> VARIANT
<222> (1)...(159)
<223> Xaa = Any Amino Acid

```

```

<400> 172
Met Val Glu Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg Pro
 1             5             10             15
Leu Leu Ala Asn Asp Leu Met Leu Ile Lys Leu Asp Glu Ser Val Ser
                20             25             30
Glu Ser Asp Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln Cys Pro Thr
                35             40             45
Ala Gly Asn Ser Cys Leu Val Ser Gly Trp Gly Leu Leu Ala Asn Gly

```


50	55	60
Arg Met Pro Thr Val Leu Gln Cys Val Asn Val Ser Val Val Ser Glu		
65	70	75
Glu Val Cys Ser Lys Leu Tyr Asp Pro Leu Tyr His Pro Ser Met Phe		80
	85	90
Cys Ala Gly Gly Gln Xaa Gln Xaa Asp Ser Cys Asn Gly Asp Ser		95
	100	105
Gly Gly Pro Leu Ile Cys Asn Gly Tyr Leu Gln Gly Leu Val Ser Phe		110
	115	120
Gly Lys Ala Pro Cys Gly Gln Val Gly Val Pro Gly Val Tyr Thr Asn		125
	130	135
Leu Cys Lys Phe Thr Glu Trp Ile Glu Lys Thr Val Gln Ala Ser		140
145	150	155

<210> 173

<211> 1265

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(1265)

<223> n = A,T,C or G

<400> 173

ggcagcccg	actgcagcc	ctggcaggcg	gcactgggtca	tggaaaacga	attgtttctgc	60
tcgggctgc	tggtgcatcc	gcagtgggtg	ctgtcagccg	cacactgttt	ccagaactcc	120
tacaccatcg	ggctgggct	gcacagtctt	gaggccgacc	aagagccagg	gagccagatg	180
gtggaggcca	gcctctccgt	acggcaccca	gagtacaaca	gaccttgc	cgctaaccgac	240
ctcatgctca	tcaagttgga	cgaatccgtg	tccgagtcctg	acaccatccg	gagcatcagc	300
attgcttcgc	agtgcctac	cgcggggaac	tcttgccctg	tttctggctg	gggtctgctg	360
gcgaacggtg	agctcacggg	tgtgtgtctg	ccctcttcaa	ggaggtccctc	tgcccagtcg	420
cgggggctga	cccagagctc	tgctcccag	gcagaatgcc	taccgtgctg	cagtgcgtga	480
acgtgtcggt	ggtgtctgag	gaggtctgca	gtaagctcta	tgacccgctg	taccacccca	540
gcatgttctg	cgccggcgga	gggcaagacc	agaaggactc	ctgcaacggt	gactctgggg	600
ggccctgat	ctgcaacggg	tacttgcaag	gccttggtgc	tttcggaaaa	gccccgtgtg	660
gccaaagtgg	cgtgccaggt	gtctacacca	acctctgcaa	attcactgag	tggatagaga	720
aaaccgtcca	ggccagttaa	ctctggggac	tgggaaccca	tgaattgac	ccccaaatac	780
atctgcgga	aggaattcag	gaatatctgt	tcccagcccc	tcctccctca	ggcccaggag	840
tccaggcccc	cagcccctcc	tccctcaaac	caagggtaca	gatccccagc	ccctcctccc	900
tcagaccag	gagtcagac	ccccagcccc	ctcctccctc	agaccagga	gtccagcccc	960
tcctccntca	gaccagagg	tccagacccc	ccagcccctc	ctccctcaga	cccaggggtt	1020
gaggccccca	acccctcctc	cttcagagtc	agaggtccaa	gcccccaacc	cctcgttccc	1080
cagaccaga	ggttnaggtc	ccagcccctc	ttccntcaga	cccagnngtc	caatgccacc	1140
tagattttcc	ctgnacacag	tgcccccttg	tggnangttg	acccaacctt	accagttggt	1200
ttttcatttt	tngtcccttt	cccctagatc	cagaaataaa	gtttaagaga	ngngcaaaaa	1260
aaaaa						1265

<210> 174

<211> 1459

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(1459)

<223> n = A,T,C or G

<400> 174

ggtcagccgc	acactgtttc	cagaagttag	tgcagagctc	ctacaccatc	gggctgggcc	60
tgcaacagtct	tgaggccgac	caagagccag	ggagccagat	gggtggaggcc	agcctctccg	120
tacggcacc	agagtacaac	agacccttgc	tcgctaacga	cctcatgctc	atcaagttgg	180
acgaatccgt	gtccgagtct	gacaccatcc	ggagcatcag	cattgcttcg	cagtgcctta	240
ccgcggggaa	ctcttgccctc	gtttctggct	ggggtctgct	ggcgaacggt	gagctcacgg	300
gtgtgtgtct	gccctcttca	aggaggtcct	ctgcccagtc	gcgggggctg	acccagagct	360
ctgctgcccc	ggcagaatgc	ctaccgtgct	gcagtgcgtg	aacgtgtcgg	tggtgtctga	420
ngaggctctgc	antaagctct	atgaccgcgt	gtaccacccc	ancatgttct	gcgcggcgcg	480
agggcaagac	cagaaggact	cctgcaacgt	gagagagggg	aaaggggagg	gcaggcgact	540
cagggaaggg	tggagaaggg	ggagacagag	acacacaggg	ccgcatggcg	agatgcagag	600
atggagagac	acacagggag	acagtgacaa	ctagagagag	aaactgagag	aaacagagaa	660
ataaacacag	gaataaagag	aagcaaagga	agagagaaac	agaaacagac	atggggaggc	720
agaaacacac	acacatagaa	atgcagttga	ccttccaaca	gcatggggcc	tgaggcggt	780
gacctccacc	caatagaaaa	tcctcttata	acttttgact	ccccaaaaac	ctgactagaa	840
atagcctact	gttgacgggg	agccttacca	ataacataaa	tagtcgattt	atgcatacgt	900
ttttatgcatt	catgatatac	ctttgttga	attttttgat	atttctaagc	tacacagttc	960
gtctgtgaat	ttttttaaat	tgttgcaact	ctcctaaaat	ttttctgatg	tgtttattga	1020
aaaaatccaa	gtataagtgg	acttgtgcat	tcaaaccagg	gttgttcaag	ggtcaactgt	1080
gtaccagag	ggaaacagtg	acacagattc	atagaggtga	aacacgaaga	gaaacaggaa	1140
aatcaagac	tctacaaaga	ggctgggcag	gggtggtcat	gcctgtaatc	ccagcacttt	1200
gggaggcgag	gcaggcagat	cacttgagggt	aaggagttca	agaccagcct	ggccaaaatg	1260
gtgaaatcct	gtctgtacta	aaaatacaaa	agttagctgg	atatgggtggc	aggcgctgt	1320
aatccagct	acttgggagg	ctgaggcagg	agaattgctt	gaatatggga	ggcagaggtt	1380
gaagttagtt	gagatcacac	cactatactc	cagctggggc	aacagagtaa	gactctgtct	1440
caaaaaaaaa	aaaaaaaaa					1459

<210> 175

<211> 1167

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(1167)

<223> n = A,T,C or G

<400> 175

ggcagccct	ggcaggcggc	actggtcatg	gaaaacgaat	tgttctgctc	gggcgtcctg	60
gtgcatccgc	agtgggtgct	gtcagccgca	cactgtttcc	agaactccta	caccatcggg	120
ctgggcctgc	acagtcttga	ggccgaccaa	gagccaggga	gccagatggt	ggaggccagc	180
ctctccgtac	ggcaccaga	gtacaacaga	ctcttgctcg	ctaacgacct	catgctcatc	240
aagttggacg	aatccgtgtc	cgagtctgac	accatccgga	gcatcagcat	tgcttcgcag	300
tgccctaccg	cggggaactc	ttgcctcgtn	tctggctggg	gtctgctggc	gaacggcaga	360
atgcctaccg	tgctgcactg	cgtagaacgtg	tcgggtggtg	ctgaggangt	ctgcagtaag	420
ctctatgacc	cgctgtacca	ccccagcatg	ttctgcgcgg	gcggaggggca	agaccagaag	480
gactcctgca	acggtgactc	tggggggccc	ctgatctgca	acgggtactt	gcagggcctt	540
gtgtctttcg	gaaaagcccc	gtgtggccaa	cttggcgctg	cagggtgtcta	caccaacctc	600
tgcaaatcca	ctgagtggat	agagaaaacc	gtccagncca	gttaactctg	gggactggga	660
acccatgaaa	ttgaccccca	aatacatcct	gcggaangaa	ttcaggaata	tctgttccca	720
gccctcctc	ctcaggccc	aggagtccag	gccccagcc	cctcctccct	caaaccaagg	780
gtacagatcc	ccagccccctc	ctccctcaga	cccaggagtc	cagaccccc	agccccctnt	840
ccntcagacc	caggagtcca	gcccctcctc	cntcagacgc	aggagtccag	acccccccagc	900
ccntcntccg	tcagacccag	gggtgcaggc	ccccaaaccc	tcntccntca	gagtcagagg	960
tcagaccccc	caaccctcgt	ttcccagac	ccagaggtnc	aggtcccagc	ccctcctccc	1020
tcagacccag	cggtccaatg	ccacctagan	tnccctgta	cacagtggcc	ccttgtggca	1080
ngttgaccca	accttaccag	ttggtttttc	attttttgtc	cctttccctt	agatccagaa	1140
ataaagtnta	agagaagcgc	aaaaaaa				1167

<210> 176
 <211> 205
 <212> PRT
 <213> Homo sapien

<220>
 <221> VARIANT
 <222> (1) ... (205)
 <223> Xaa = Any Amino Acid

<400> 176
 Met Glu Asn Glu Leu Phe Cys Ser Gly Val Leu Val His Pro Gln Trp
 1 5 10 15
 Val Leu Ser Ala Ala His Cys Phe Gln Asn Ser Tyr Thr Ile Gly Leu
 20 25 30
 Gly Leu His Ser Leu Glu Ala Asp Gln Glu Pro Gly Ser Gln Met Val
 35 40 45
 Glu Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg Leu Leu Leu
 50 55 60
 Ala Asn Asp Leu Met Leu Ile Lys Leu Asp Glu Ser Val Ser Glu Ser
 65 70 75 80
 Asp Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln Cys Pro Thr Ala Gly
 85 90 95
 Asn Ser Cys Leu Val Ser Gly Trp Gly Leu Leu Ala Asn Gly Arg Met
 100 105 110
 Pro Thr Val Leu His Cys Val Asn Val Ser Val Val Ser Glu Xaa Val
 115 120 125
 Cys Ser Lys Leu Tyr Asp Pro Leu Tyr His Pro Ser Met Phe Cys Ala
 130 135 140
 Gly Gly Gly Gln Asp Gln Lys Asp Ser Cys Asn Gly Asp Ser Gly Gly
 145 150 155 160
 Pro Leu Ile Cys Asn Gly Tyr Leu Gln Gly Leu Val Ser Phe Gly Lys
 165 170 175
 Ala Pro Cys Gly Gln Leu Gly Val Pro Gly Val Tyr Thr Asn Leu Cys
 180 185 190
 Lys Phe Thr Glu Trp Ile Glu Lys Thr Val Gln Xaa Ser
 195 200 205

<210> 177
 <211> 1119
 <212> DNA
 <213> Homo sapien

<400> 177
 ggcgactcgc agccctggca ggcggcactg gtcattggaaa acgaattggt ctgctcgggc 60
 gtccctggtgc atccgcagtg ggtgctgtca gccgcacact gttccagaa ctccacacc 120
 atcgggctgg gctgcacag tcttgaggcc gaccaagagc caggagacca gatggtggag 180
 gccagcctct ccgtacggca cccagagtac aacagaccct tgctcgctaa cgacctcatg 240
 ctcatcaagt tggacgaatc cgtgtccgag tctgacacca tccggagcat cagcattgct 300
 tcgcagtgcc ctaccgcggg gaactcttgc ctgcgttctg gctggggtct gctggcgaaac 360
 gatgctgtga ttgccatcca gtcccagact gtgggaggct gggagtgtga gaagctttcc 420
 caaccctggc aggggtgtac catttcggca acttccagt caaggacgtc ctgctgcac 480
 ctactggtg gctcactact gctcactgca tcaccggaa cactgtgat aactagccag 540
 caccatagtt ctccgaagtc agactatcat gattactgtg ttgactgtgc tgtctattgt 600
 actaaccatg ccgatgttta ggtgaaatta gcgtcacttg gcctcaacca tcttggtatc 660
 cagttatcct cactgaattg agatttctg cttcagtgtc agccattccc acataatttc 720
 tgacctacag aggtgaggga tcatatagct cttcaaggat gctggtactc ccctcacaaa 780

```

ttcattttctc ctgtttagt gaaaggtgcg ccctctggag cctcccaggg tgggtgtgca      840
ggtcacaatg atgaatgtat gatcgtgttc ccattacca aagcctttaa atccctcatg      900
ctcagtacac cagggcaggt ctagcatttc ttcatttagt gtatgctgtc cattcatgca      960
accacctcag gactcctgga ttctctgect agttgagctc ctgcatgctg cctccttggg     1020
gaggtgaggg agagggccca tggttcaatg ggatctgtgc agttgtaaca cattaggtgc     1080
ttaataaaca gaagctgtga tgtaaaaaa aaaaaaaaaa     1119

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<210> 178
<211> 164
<212> PRT
<213> Homo sapien

<220>
<221> VARIANT
<222> (1)...(164)
<223> Xaa = Any Amino Acid

```

```

<400> 178
Met Glu Asn Glu Leu Phe Cys Ser Gly Val Leu Val His Pro Gln Trp
 1          5          10          15
Val Leu Ser Ala Ala His Cys Phe Gln Asn Ser Tyr Thr Ile Gly Leu
 20          25          30
Gly Leu His Ser Leu Glu Ala Asp Gln Glu Pro Gly Ser Gln Met Val
 35          40          45
Glu Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg Pro Leu Leu
 50          55          60
Ala Asn Asp Leu Met Leu Ile Lys Leu Asp Glu Ser Val Ser Glu Ser
 65          70          75          80
Asp Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln Cys Pro Thr Ala Gly
 85          90          95
Asn Ser Cys Leu Val Ser Gly Trp Gly Leu Leu Ala Asn Asp Ala Val
100          105          110
Ile Ala Ile Gln Ser Xaa Thr Val Gly Gly Trp Glu Cys Glu Lys Leu
115          120          125
Ser Gln Pro Trp Gln Gly Cys Thr Ile Ser Ala Thr Ser Ser Ala Arg
130          135          140
Thr Ser Cys Cys Ile Leu Thr Gly Cys Ser Leu Leu Thr Ala Ser
145          150          155          160
Pro Gly Thr Leu

```

```

<210> 179
<211> 250
<212> DNA
<213> Homo sapien

```

```

<400> 179
ctggagtgcc ttggtgtttc aagcccctgc aggaagcaga atgcaccttc tgaggcacct      60
ccagctgccc ccggccgggg gatgcgaggc tcggagcacc cttgcccggc tgtgattgct     120
gccaggcact gttcatctca gcttttctgt ccctttgctc ccggcaagcg cttctgctga     180
aagttcatat ctggagcctg atgtcttaac gaataaaggt cccatgctcc acccgaaaaa     240
aaaaaaaaaa                                     250

```

```

<210> 180
<211> 202
<212> DNA
<213> Homo sapien

```

<400> 180
 actagtcag tgtggtggaa ttccattgtg ttgggcccac cacaatggct acctttaaca 60
 tcacccagac cccgcccctg cccgtgcccc acgtgctgc taacgacagt atgatgctta 120
 ctctgctact cggaaactat ttttatgtaa ttaatgtatg ctttcttgtt tataaatgcc 180
 tgatttaaaa aaaaaaaaaa aa 202

<210> 181
 <211> 558
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1) ... (558)
 <223> n = A,T,C or G

<400> 181
 tccytttgkt naggtttkkg agacamccck agacctwaan ctgtgtcaca gacttcyngg 60
 aatgtttagg cagtgtcagt aatttcytcg taatgattct gttattactt tccnattct 120
 ttattcctct ttcttctgaa gattaatgaa gttgaaaatt gaggtggata aatacaaaaa 180
 ggtagtgtga tagtataagt atctaagtgc agatgaaagt gtgttatata tatccattca 240
 aaattatgca agttagtaat tactcagggt taactaaatt actttaatat gctgttgaac 300
 ctactctgtt ccttggtctag aaaaaattat aaacaggact ttgttagttt gggaaagccaa 360
 attgataata ttctatgttc taaaagtgtg gctatacata aattattaag aaatatggaw 420
 ttttatcccc aggaatatgg kgttcatttt atgaatatta cscrggatag awgtwtgagt 480
 aaaaycagtt ttggtwaata ygtwaatatg tcmtaaataa acaakgcttt gacttatttc. 540
 caaaaaaaaa aaaaaaaaaa 558

<210> 182
 <211> 479
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1) ... (479)
 <223> n = A,T,C or G

<400> 182
 acagggwttk grggatgcta agsccccrga rwtggtttga tccaaccctg gcttwttttc 60
 agaggggaaa atggggccta gaagttacag mscatytagy tgggtgcmtg gcacccctgg 120
 cstcacacag astcccaggt agctgggact acaggcacac agtcactgaa gcaggccctg 180
 ttwgcaattc acgttgccac ctccaactta aacattcttc atatgtgatg tccttagtca 240
 ctaaggttaa actttcccac ccagaaaagg caacttagat aaaatcttag agtactttca 300
 tactmttcta agtctctctc cagcctcact kkgagtccctm cytggggggt gataggaant 360
 ntctcttggc tttctcaata aartctctat ycatctcatg tttaatttgg tacgcatara 420
 awtgstgata aaattaaaat gttctggtty mactttaaaa aaaaaaaaaa aaaaaaaaaa 479

<210> 183
 <211> 384
 <212> DNA
 <213> Homo sapien

<400> 183
 aggcgggagc agaagctaaa gccaaagccc aagaagagtg gcagtgccag cactggtgcc 60
 agtaccagta ccaataacag tgccagtgcc agtgccagca ccagtgggtg cttcagtgct 120
 ggtgccagcc tgaccgccac tctcacattt gggctcttcg ctggccttgg tggagctgg 180
 gccagcacca gtggcagctc tgggtgcctgt ggtttctcct acaagtgaga ttttagatat 240

tgттаатсст gccagtcttt ctcttcaagc caggggtgcat cctcagaaac ctactcaaca	300
cagcactcta ggcagccact atcaatcaat tgaagttgac actctgcatt aratctattt	360
gccatttcaa aaaaaaaaaa aaaa	384

<210> 184
 <211> 496
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(496)
 <223> n = A,T,C or G

<400> 184		
accgaattgg gaccgctggc ttataagcga tcatgtyynt ccrgtatcac ctcaacgagc	60	
agggagatcg agtctatacg ctgaagaaat ttgacccgat gggacaacag acctgctcag	120	
cccatcctgc tcggttctcc ccagatgaca aatactctsg acaccgaatc accatcaaga	180	
aacgcttcaa ggtgctcatg acccagcaac cgcgcctgt cctctgaggg tcccttaaac	240	
tgatgtcttt tctgccacct gttacccctc ggagactccg taaccaaact cttcggactg	300	
tgagccctga tgcctttttg ccagccatac tctttggcat ccagtctctc gtggcgattg	360	
attatgcttg tgtgaggcaa tcatggtggc atcacccata aagggaacac atttgacttt	420	
tttttctcat attttaaat actacmagaw tattwmagaw waaatgawtt gaaaaactst	480	
taaaaaaaaa aaaaaa	496	

<210> 185
 <211> 384
 <212> DNA
 <213> Homo sapien

<400> 185		
gctggtagcc tatggcgkkg cccacggagg ggctcctgag gccacggrac agtgacttcc	60	
caagtatcyt gcgscgctc ttctaccgtc cctacctgca gatcttcggg cagattcccc	120	
aggaggacat ggacgtggcc ctcatggagc acagcaactg ytcgtcggag cccggcttct	180	
gggcacaccc tcttgggggc caggcgggca cctgcgtctc ccagtatgcc aactggtctg	240	
tgggtgctgt cctcgtcatc ttctgctcg tggccaacat cctgctggtc aacttgctca	300	
ttgcatgtt cagttacaca ttcggcaaaag tacagggcaa cagcgatctc tactgggaag	360	
gcgcagcgtt accgcctcat ccgg	384	

<210> 186
 <211> 577
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(577)
 <223> n = A,T,C or G

<400> 186		
gagttagctc ctccacaacc ttgatgaggt cgtctgcagt ggcctctcgc ttcataccgc	60	
tnccatcgte atactgtagg ttgccaacca cytctctggc tcttggggcg gcntaatatt	120	
ccaggaaact ctcaatcaag tcaccgtcga tgaaacctgt gggctgggtc tgtcttcgcg	180	
tcggtgtgaa aggatctccc agaaggagtg ctcgatcttc cccacacttt tgatgacttt	240	
attgagtcga ttctgcatgt ccagcaggag gttgtaccag ctctctgaca gtgaggtcac	300	
cagccctatc atgcccgtga mcgtgccgaa garcaccgag ccttggtgtg gggkkgaagt	360	
ctcaccaga ttctgcatta ccagagagcc gtggcaaaag acattgacaa actcgcccag	420	
gtggaaaaag amcamctcct ggargtgctn gccgctctc gtcmggttgt ggcagcgctw	480	

tccttttgac acacaaacaa gttaaaggca ttttcagccc ccagaaantt gtcacatccc 540
aagatntcgc acagcactna tccagttggg attaaat 577

<210> 187
<211> 534
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(534)
<223> n = A,T,C or G

<400> 187
aacatcttcc tgtataatgc tgtgtaatat cgatccgatn ttgtctgstg agaaticatw 60
actkggaaaa gmaacattaa agcctggaca ctggtattaa aattcacaat atgcaacact 120
ttaaacagtg tgtcaatctg ctcccyynac tttgtcatca ccagtctggg aakaagggta 180
tgccctattc acacctgtta aaagggcgct aagcattttt gattcaacat cttttttttt 240
gacacaagtc cgaaaaaagc aaaagtaaac agttatyaat ttgttagcca attcactttc 300
ttcatgggac agagccatyt gatttaaaaa gcaaattgca taatattgag cttggggagc 360
tgatatttga gcggaagagt agcctttcta cttcaccaga cacaactccc tttcatattg 420
ggatgttnac naaagtwatg tctctwacag atgggatgct tttgtggcaa tttgtttctg 480
aggatctccc agtttattta ccacttgcac aagaaggcgt tttcttcttc aggc 534

<210> 188
<211> 761
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(761)
<223> n = A,T,C or G

<400> 188
agaaaccagt atctctnaaa acaacctctc ataccttctg gacctaattt tgtgtgcgtg 60
tgtgtgtgcg cgcataattat atagacaggc acatcttttt tacttttgta aaagcttatg 120
cctctttggt atctatatct gtgaaagttt taatgatctg ccataatgtc ttggggacct 180
ttgtcttctg tgtaaatggt actagagaaa acacctatnt tatgagtcaa tctagttngt 240
tttattcgac atgaaggaaa tttccagatn acaacactna caaactctcc ctkgackarg 300
ggggacaaag aaaagcaaaa ctgamcataa raaacaatwa cctggtgaga arttgcataa 360
acagaaatwr ggtagtatat tgaarnacag catcattaaa rmgttwtktt wttctccctt 420
gcaaaaaaca tgtacngact tcccgttgag taatgccaaag ttgttttttt tatnataaaa 480
cttgcccttc attacatggt tnaaagtggg gtggtgggcc aaaatattga aatgatggaa 540
ctgactgata aagctgtaca aataagcagt gtgcctaaca agcaacacag taatgttgac 600
atgcttaatt cacaaatgct aatttcatta taaatgtttg ctaaaataca ctttgaacta 660
tttttctgtn ttcccagagc tgagatntta gattttatgt agtatnaagt gaaaaantac 720
gaaaataata acattgaaga aaaaanaaaa aaanaaaaaa a 761

<210> 189
<211> 482
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(482)
<223> n = A,T,C or G

<400> 189
tttttttttt tttgccgatn ctactatttt attgcaggan gtgggggtgt atgcaccgca 60
caccggggct atnagaagca agaaggaagg agggagggca cagccccttg ctgagcaaca 120
aagccgcctg ctgccttctc tgtctgtctc ctggtgcagg cacatgggga gaccttcccc 180
aaggcagggg ccaccagtcc aggggtggga atacaggggg tgggangtgt gcataagaag 240
tgataggcac aggccacccg gtacagaccc ctcggtcctt gacaggtnga tttcgaccag 300
gtcattgtgc cctgcccagg cacagcgtan atctggaaaa gacagaatgc tttccttttc 360
aaatttggct ngtcatngaa ngggcanttt tccaanttng gctnggtctt ggtacncttg 420
gttcggccca gtcncnctc caaaaantat tcacccnctt cnaattgct tgcnngnccc 480
cc 482

<210> 190
<211> 471
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(471)
<223> n = A,T,C or G

<400> 190
tttttttttt ttttaaaaca gtttttcaca acaaaattta ttagaagaat agtgggtttt 60
aaaactctcg catccagtga gaactacat acaccacatt acagctngga atgtntccca 120
aatgtctggt caaatgatac aatggaacca ttcaatctta cacatgcacg aaagaacaag 180
cgcttttgac atacaatgca caaaaaaaaa aggggggggg gaccacatgg attaaaattt 240
taagtactca tcacatacat taagacacag ttctagtcca gtcnaaaatc agaactgcnt 300
tgaaaaattt catgtatgca atccaaccaa agaacttnat tggatgatcat gantnctcta 360
ctacatcnac cttgatcatt gccaggaacn aaaagttnaa ancacncngt acaaaaanaa 420
tctgtaattn anttcaacct ccgtacngaa aaatnttntt tatacactcc c 471

<210> 191
<211> 402
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(402)
<223> n = A,T,C or G

<400> 191
gagggattga aggtctgttc tastgtcggm ctgttcagcc accaactcta acaagttgct 60
gtcttccact cactgtctgt aagcttttta acccagacwg tatcttcata aatagaacaa 120
attcttcacc agtcacatct tctaggacct ttttggtatc agttagtata agctcttcca 180
cttcttttgt taagacttca tctggtaaag tcttaagttt ttagaaaagg aattyaattg 240
ctcgttctct aacaatgtcc tctccttgaa gtatttggct gaacaaccca cctaaagtcc 300
ctttgtgcat ccatttttaa tatacttaat agggcattgk tncactaggt taaattctgc 360
aagagtcatc tgtctgcaaa agttgcgtta gtatatctgc ca 402

<210> 192
<211> 601
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature

<222> (1)...(601)

<223> n = A,T,C or G

<400> 192.

gagctcggat	ccaataatct	ttgtctgagg	gcagcacaca	tatncagtgc	catggnaact	60
ggtctacccc	acatgggagc	agcatgccgt	agntatataa	ggtcattccc	tgagtcagac	120
atgcytyttt	gaytaccgtg	tgccaagtgc	tggtgattct	yaacacacyt	ccatcccgyt	180
cttttggtga	aaaactggca	cttkcttgga	actagcarga	catcacttac	aaattcaccc	240
acgagacact	tgaaagggtg	aacaaagcga	ytcttgcaat	gctttttgtc	cctccggcac	300
cagttgtcaa	tactaaccgc	ctggtttgcc	tccatcacat	ttgtgatctg	tagctctgga	360
tacatctcct	gacagtactg	aagaacttct	tcttttgttt	caaaagcacc	tcttggtgcc	420
tggtggatca	ggttcccatt	tcccagtcyg	aatgttcaca	tggcataatt	wacttcccac	480
aaaacattgc	gatttgaggc	tcagcaacag	caaatcctgt	tccggcattg	gctgcaagag	540
cctcgatgta	gccggccagc	gccaaaggcag	gcgcctgtgag	ccccaccagc	agcagaagca	600
g						601

<210> 193

<211> 608

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(608)

<223> n = A,T,C or G

<400> 193

atacagccca	natcccacca	cgaagatgcg	cttggtgact	gagaacctga	tgcggtcact	60
ggteccgctg	tagccccagc	gactctccac	ctgctggaag	cggttgatgc	tgactcyyt	120
cccaacgcag	gcagmagcgg	gsccggtcaa	tgaactccay	tcgtggcttg	gggtkgacgg	180
tkaagtgcag	gaagaggctg	accacctcgc	ggteccaccag	gatgcccagc	tgteggggac	240
ctgcagcgaa	actcctcgat	ggtecatgagc	gggaagcgaa	tgaggcccag	ggccttgccc	300
agaaccttcc	gcctgttctc	tggcgtcacc	tgacgtgct	gccgctgaca	ctcggcctcg	360
gaccagcgga	caaacggcrt	tgaacagccg	cacctcacgg	atgccacgtg	tgtecgctc	420
caggamngsc	accagcgtgt	ccaggtcaat	gtcggtgaag	ccctccgcgg	gtrattggcgt	480
ctgcagtggt	tttgtcgatg	ttctccaggc	acaggctggc	cagctgcggg	tcacgaaga	540
gtcgcgcctg	cgtgagcagc	atgaaggcgt	tgteggctcg	cagttcttct	tcaggaaactc	600
cacgcaat						608

<210> 194

<211> 392

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(392)

<223> n = A,T,C or G

<400> 194

gaacggctgg	acctgacctc	gcattgtgct	tgctggcagg	gaataccttg	gcaagcagyt	60
ccagtcgcag	cagccccaga	ccgctgccgc	ccgaagctaa	gcctgcctct	ggccttcccc	120
tccgcctcaa	tgacagaacca	gtagtgggag	cactgtgttt	agagttaaga	gtgaacactg	180
tttgatttta	cttgggaatt	tcctctgtta	tatagctttt	cccaatgcta	atttccaaac	240
aacaacaaca	aaataacatg	tttgctgtt	aagtgtgata	aaagtaggtg	attctgtatt	300
taaagaaaat	attactgtta	catatactgc	ttgcaatttc	tgtattttatt	gktnctstgg	360
aaataaatat	agttattaaa	ggttgtcant	cc			392

<210> 195
 <211> 502
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(502)
 <223> n = A,T,C or G

<400> 195
 ccsttkgagg ggtkaggkyc cagttyccga gtggaagaaa caggccagga gaagtgcgtg 60
 ccgagctgag gcagatgttc ccacagtgc cccagagcc stgggstata gtytctgacc 120
 cctcncaagg aaagaccacs ttctggggac atgggctgga gggcaggacc tagaggcacc 180
 aagggaaggc cccattccgg ggstgttccc cgaggaggaa ggggaagggc tctgtgtgcc 240
 ccccasgagg aagaggccct gagtccctggg atcagacacc ccttcacgtg tatccccaca 300
 caaatgcaag ctcaccaagg tcccctctca gtccccttcc stacaccctg amcggccact 360
 gscscacacc caccagagc acgccaccgc ccatggggar tgtgtcaag gartcgcnng 420
 gcargctgga catctngtcc cagaaggggg cagaatctcc aatagangga ctgarcmstt 480
 gctnanaaaa aaaaanaaaa aa 502

<210> 196
 <211> 665
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(665)
 <223> n = A,T,C or G

<400> 196
 ggttacttgg ttctattgcc accacttagt ggatgtcatt tagaaccatt ttgtctgctc 60
 cctctggaag ccttgccgag agcggacttt gtaattgttg gagaataact gctgaatttt 120
 wagctgtttk gagtgtgatts gcaccactgc acccacaact tcaatatgaa aacyawttga 180
 actwatattat tatcttgtga aaagtataac aatgaaaatt ttgttcatac tgtattkac 240
 aagtatgatg aaaagcaawa gatataatatt cttttattat gttaaattat gattgccatt 300
 attaatcggc aaaaatgtgga gtgtatgttc ttttcacagt aatataatgcc ttttgtaact 360
 tcacttggtt attttattgt aaatgartta caaaattcctt aatttaagar aatggatgt 420
 watatttatt tcattaattt ctttcctkgt ttacgtwaat tttgaaaaga wtgcatgatt 480
 tcttgacaga aatcgatctt gatgctgtgg aagtagtttg acccacatcc ctatgagttt 540
 ttcttagaat gtataaagggt tgtagcccat cnaacttcaa agaaaaaat gaccacatac 600
 tttgcaatca ggctgaaatg tggcatgctn ttctaattcc aactttataa actagcaaan 660
 aagtg 665

<210> 197
 <211> 492
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(492)
 <223> n = A,T,C or G

<400> 197
 tttntttttt ttttttttgc aggaaggatt ccatattattg tggatgcatt ttcacaatat 60
 atgtttattg gagcgatcca ttatcagtga aaagtatcaa gtgtttataa natttttagg 120

```

aaggcagatt cacagaacat gctngtcngc ttgcagtttt acctcgtana gatnacagag      180
aattatagtc naaccagtaa acnaggaatt tacttttcaa aagattaaat ccaaactgaa      240
caaaattcta ccctgaaact tactccatcc aaatattgga ataanagtca gcagtgatac      300
attctcttct gaactttaga ttttctagaa aaatatgtaa tagtgatcag gaagagctct      360
tgttcaaaaag tacaacnaag caatgttccc ttaccatagg ccttaattca aactttgatc      420
catttcactc ccatcacggg agtcaatgct acctgggaca cttgtatttt gtcatnctg      480
ancntggctt aa                                                              492

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<210> 198
<211> 478
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(478)
<223> n = A,T,C or G

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<400> 198
ttnttttgn atttcantct gtannaanta ttttcattat gtttattana aaaatatnaa      60
tgtntccacn acaaatcatn ttacntnagt aagagggcan ctacattgta caacatacac      120
tgagtatatt ttgaaaagga caagttttaa gtanacncat attgccganc atancacatt      180
tatacatggc ttgattgata ttttagcacag canaaactga gtgagttacc agaaanaaat      240
natatatgtc aatcngatth aagatacaaa acagatccta tgggtacatan catcntgtag      300
gagttgtggc tttatgttta ctgaaagtca atgcagttcc tgtacaaaga gatggccgta      360
agcattctag tacctctact ccatgggtaa gaatcgtaca cttatgttta catatgtnc      420
gggtaagaat tgtgttaagt naanttatgg agaggtccan gagaaaaatt tgatncaa      478

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<210> 199
<211> 482
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(482)
<223> n = A,T,C or G

```

```

<400> 199
agtgacttgt cctccaacaa aaccccttga tcaagtttgt ggcactgaca atcagaccta      60
tgctagttcc tgtcatctat tcgtactaa atgcagactg gaggggacca aaaaggggca      120
tcaactccag ctggattatt ttggagcctg caaatctatt cctacttgta cggactttga      180
agtgattcag tttcctctac ggatgagaga ctggctcaag aatatectca tgcagcttta      240
tgaagccnac tctgaacacg ctggttatct nagatgagaa ncagagaaat aaagtcnaga      300
aaatttacct ggangaaaag aggccttngg ctggggacca tccattgaa ccttctctta      360
anggacttta agaanaaaact accacatgtn tgnngtatcc tgggtgccngg ccgtttantg      420
aacntngacn ncacccctnt ggaatanant cttgaacngn tcctgaactt gctcctctgc      480
ga                                                              482

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<210> 200
<211> 270
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(270)
<223> n = A,T,C or G

```

<400> 200
 cggccgcaag tgcaactcca gctggggccg tgcggaacgaa gattctgcca gcagttggtc 60
 cgactgcgac gacggcggcg gcgacagtcg cagggtgcagc gcgggcgcct ggggtcttgc 120
 aaggctgagc tgacgcccga gaggtcgtgt cacgtccac gaccttgacg ccgtcgggga 180
 cagccggaac agagcccggt gaangcggga ggcctcgggg agcccctcgg gaagggcggc 240
 ccgagagata cgcaggtgca ggtggccgcc 270

<210> 201
 <211> 419
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(419)
 <223> n = A,T,C or G

<400> 201
 tttttttttt ttttgaatc tactgcgagc acagcaggtc agcaacaagt ttattttgca 60
 gctagcaagg taacagggtg gggcatggtt acatgttcag gtcaacttcc tttgtcgtgg 120
 ttgattggtt tgtctttatg ggggcggggg ggggtagggg aaancgaagc anaantaaca 180
 tggagtgggt gcaccctccc tgtagaacct gggtacnaaa gcttggggca gttcacctgg 240
 tctgtgaccg tcattttctt gacatcaatg ttattagaag tcaggatata ttttagagag 300
 tccactgtnt ctggaggag attagggttt cttgccaana tccaancaa atccacntga 360
 aaaagtggga tgatncangt acngaatacc ganggcatan ttctcatant cggtggcc 419

<210> 202
 <211> 509
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(509)
 <223> n = A,T,C or G

<400> 202
 tttntttttt tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt 60
 tggcacttaa tccattttta tttcaaaatg tctacaaant ttnaatncnc cattatacng 120
 gtnattttnc aaaatctaaa nnttattcaa atntnagcca aantccttac ncaaattnaa 180
 tacnncnaaa aatcaaaaat atacntntct ttcagcaaac ttngttacat aaattaaaaa 240
 aatatatacg gctgggtgtt tcaaagtaca attatcttaa cactgcaaac atnttttnaa 300
 ggaactaaaa taaaaaaaaa cactnccgca aaggttaaag ggaacaacaa attcntttta 360
 caacancnnc nattataaaa atcatatctc aaatcttagg ggaatatata cttcacacng 420
 ggatcttaac ttttactnca ctttgtttat ttttttanaa ccattgtntt gggcccaaca 480
 caatggnaat nccnccnncn tgactagt 509

<210> 203
 <211> 583
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(583)
 <223> n = A,T,C or G

```

<400> 203
tttttttttt ttttttttga cccccctctt ataaaaaaca agttaccatt ttatttttact    60
tacacatatt ttttttataa ttggtattag atattcaaaa ggcagctttt aaaatcaaac    120
taaatggaaa ctgccttaga tacataattc ttaggaatta gcttaaaatc tgcctaaagt    180
gaaaatcttc tctagctctt ttgactgtaa atttttgact cttgtaaaac atccaaattc    240
atttttcttg tctttaaaat tatctaattc ttccattttt tccctattcc aagtcaattt    300
gcttctctag cctcatttcc tagctcttat ctactattag taagtggctt ttttcctaaa    360
agggaaaaca ggaagagana atggcacaca aaacaaacat tttatattca tttttctacc    420
tacgttaata aaatagcatt ttgtgaagcc agctcaaaaag aaggcttaga tccttttatg    480
tccattttag tcactaaacg atatcnaaag tgccagaatg caaaagggtt gtgaacattt    540
attcaaaagc taatataaga tttttcacat actcatcttt ctg                    583

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<210> 204
<211> 589
<212> DNA
<213> Homo sapien

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<220>
<221> misc_feature
<222> (1)...(589)
<223> n = A,T,C or G

```

```

<400> 204
ttttttttnt tttttttttt ttttttntct ttcttttttt ttganaatga ggatcgagtt    60
tttactcttc tagatagggc atgaagaaaa ctcatctttc cagcttttaa ataacaatca    120
aatctcttat gctatatcat attttaagtt aaactaatga gtcactggct tatcttctcc    180
tgaaggaaat ctgttcattc ttctcattca tatagttata tcaagtacta ccttgcatat    240
tgagagggtt ttcttctcta ttacacata tttttccatg tgaatttgta tcaaaccttt    300
attttcatgc aaactagaaa ataatgtntt cttttgcata agagaagaga acaatatnag    360
cattacaaaa ctgctcaaat tgtttgtaa gnttatccat tataattagt tnggcaggag    420
ctaatacaaa tcacatttac ngacnagcaa taataaaact gaagtaccag ttaaatatcc    480
aaaaataatta aaggaacatt ttagcctgg gtataattag ctaattcact ttacaagcat    540
ttattnagaa tgaattcaca tgttattatt centagccca acacaatgg                    589

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<210> 205
<211> 545
<212> DNA
<213> Homo sapien

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<220>
<221> misc_feature
<222> (1)...(545)
<223> n = A,T,C or G

```

```

<400> 205
ttttnttttt ttttttcagt aataatcaga acaatattta tttttatatt taaaattcat    60
agaaaagtgc cttacattta ataaaagttt gtttctcaaa gtgatcagag gaattagata    120
tngtcttgaa caccaatatt aatttgagga aaataacca aaatacatta agtaaattat    180
ttaagatcat agagcttgta agtgaaaaga taaaatttga cctcagaaac tctgagcatt    240
aaaaatccac tattagcaaa taaattacta tggacttctt gctttaattt tgtgatgaat    300
atggggtgtc actggtaaac caacacattc tgaaggatac attacttagt gatagattct    360
tatgtacttt gctanatnac gtggatatga gttgacaagt ttctctttct tcaatctttt    420
aaggggcnng ngaaatgagg aagaaaagaa aaggattacg catactgttc tttctatngg    480
aaggattaga tatgtttcct ttgccaatat taaaaaata ataatgttta ctactagtga    540
aacc

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<210> 206
<211> 487

```

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (487)

<223> n = A,T,C or G

<400> 206

tttttttttt	tttttttagtc	aagtttctna	tttttattat	aattaaagtc	ttggtcattt	60
catttattag	ctctgcaact	tacatattta	aattaaagaa	acgttnttag	acaactgtna	120
caatttataa	atgtaagggtg	ccattattga	gtanatatat	tcctccaaga	gtggatgtgt	180
cccttctccc	accaactaat	gaancagcaa	cattagttta	attttattag	tagatnatac	240
actgctgcaa	acgctaattc	tcttctccat	ccccatgtng	atattgtgta	tatgtgtgag	300
ttggttagaa	tgcatacanca	atctnacaat	caacagcaag	atgaagctag	gcntgggctt	360
tcggtgaaaa	tagactgtgt	ctgtctgaat	caaatgatct	gacctatcct	cggtggcaag	420
aactcttcga	accgcttcct	caaaggcngc	tgccacattt	gtggcctctn	ttgcacttgt	480
ttcaaaa						487

<210> 207

<211> 332

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (332)

<223> n = A,T,C or G

<400> 207

tgaattggct	aaaagactgc	atttttanaa	ctagcaactc	ttatttcttt	cctttaaaaa	60
tacatagcat	taaatcccaa	atcctattta	aagacctgac	agcttgagaa	ggctcactact	120
gcatttatag	gaccttctgg	tggttctgct	gttacntttg	aantctgaca	atccttgana	180
atctttgcat	gcagaggagg	taaaagggtat	tggattttca	cagaggaana	acacagcgca	240
gaaatgaagg	ggccaggctt	actgagcttg	tccactggag	ggctcatggg	tgggacatgg	300
aaaagaaggc	agcctaggcc	ctggggagcc	ca			332

<210> 208

<211> 524

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (524)

<223> n = A,T,C or G

<400> 208

agggcggtgt	gcggagggcg	ttactgtttt	gtctcagtaa	caataaatac	aaaaagactg	60
gttgtgttcc	ggccccatcc	aaccacgaag	ttgatttctc	ttgtgtgcag	agtgactgat	120
tttaaaggac	atggagcttg	tcacaatgtc	acaatgtcac	agtggtgaagg	gcacactcac	180
tcccgcgtga	ttcacattta	gcaaccaaca	atagctcatg	agtccatact	tgtaaatact	240
tttggcagaa	tacttnttga	aacttgcaga	tgataactaa	gatccaagat	atttcccaaa	300
gtaaatagaa	gtgggtcata	atattaatta	cctgttcaca	tcagcttcca	tttacaagtc	360
atgagccag	acactgacat	caaactaagc	ccacttagac	tcctcaccac	cagtctgtcc	420
tgtcatcaga	caggaggctg	tcaccttgac	caaatttcca	ccagtcaatc	atctatccaa	480
aaaccattac	ctgatccact	tccggtaatg	caccaccttg	gtga		524

<210> 209
 <211> 159
 <212> DNA
 <213> Homo sapien

<400> 209
 ggggtgaggaa atccagagtt gccatggaga aaattccagt gtcagcatte ttgctccttg 60
 tggccctctc ctacactctg gccagagata ccacagtcaa acctggagcc aaaaaggaca 120
 caaaggactc tcgacccaaa ctgccccaga ccctctcca 159

<210> 210
 <211> 256
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1) ... (256)
 <223> n = A,T,C or G

<400> 210
 actccctggc agacaaaggc agaggagaga gctctgtag ttctgtgttg ttgaactgcc 60
 actgaatttc ttccacttg gactattaca tgccanttga gggactaatg gaaaaacgta 120
 tggggagatt ttanccaatt tangtntgta aatggggaga ctggggcagg cgggagagat 180
 ttgcaggggtg naaatgggan ggctggtttg ttanatgaac agggacatag gaggtaggca 240
 ccaggatgct aaatca 256

<210> 211
 <211> 264
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1) ... (264)
 <223> n = A,T,C or G

<400> 211
 acattgtttt tttagataa agcattgaga gagctctcct taacgtgaca caatggaagg 60
 actggaacac ataccacat ctttgttctg agggataatt ttctgataaa gtcttgctgt 120
 atattcaagc acatatgtta tatattattc agttccatgt ttatagccta gttaaggaga 180
 ggggagatac attcngaaag aggactgaaa gaaatactca agtnggaaaa cagaaaaaga 240
 aaaaaaggag caaatgagaa gcct 264

<210> 212
 <211> 328
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1) ... (328)
 <223> n = A,T,C or G

<400> 212
 acccaaaaat ccaatgctga atatttggtc tcattattcc canattcttt gattgtcaaa 60
 ggatttaatg ttgtctcagc ttgggcactt cagttaggac ctaaggatgc cagccggcag 120
 gtttatatat gcagcaacaa tattcaagcg cgacaacagg ttattgaact tgcccgccag 180

ttnaatttca	ttccattga	cttgggatcc	ttatcatcag	ccagagagat	tgaaaattta	240
cccctaenac	tctttactct	ctgganaggg	ccagtgggtgg	tagctataag	cttggccaca	300
tttttttttc	ctttattcct	ttgtcaga				328

<210> 213
 <211> 250
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(250)
 <223> n = A,T,C or G

<400> 213						
acttatgagc	agagcgacat	atccnagtgt	agactgaata	aaactgaatt	ctctccagtt	60
taaagcattg	ctcactgaag	ggatagaagt	gactgccagg	agggaaagta	agccaaggct	120
cattatgccca	aagganatat	acattttcaat	tctccaaact	tcttcctcat	tccaagagtt	180
ttcaatattt	gcatgaacct	gctgataanc	catgttaana	aacaaatata	tctctnacct	240
tctcatcggt						250

<210> 214
 <211> 444
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(444)
 <223> n = A,T,C or G

<400> 214						
accagaatc	caatgctgaa	tatttggtt	cattattccc	agattctttg	attgtcaaag	60
gatttaagt	tgtctcagct	tgggcacttc	agttaggacc	taaggatgcc	agccggcagg	120
tttatatatg	cagcaacaat	attcaagcgc	gacaacaggt	tattgaactt	gcccgccagt	180
tgaatttcat	tccattgac	ttgggatcct	tatcatcagc	canagagatt	gaaaatttac	240
ccctacgact	ctttactctc	tggagagggc	cagtgggtgg	agctataagc	ttggccacat	300
ttttttttcc	ttttattcct	tgtcagagat	gcgattcata	catatgctan	aaaccaacag	360
agtgactttt	acaaaattcc	tataganatt	gtgaataaaa	ccttacctat	agttgccatt	420
actttgctct	ccctaataata	cctc				444

<210> 215
 <211> 366
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(366)
 <223> n = A,T,C or G

<400> 215						
acttatgagc	agagcgacat	atccaagtgt	anactgaata	aaactgaatt	ctctccagtt	60
taaagcattg	ctcactgaag	ggatagaagt	gactgccagg	agggaaagta	agccaaggct	120
cattatgccca	aagganatat	acattttcaat	tctccaaact	tcttcctcat	tccaagagtt	180
ttcaatattt	gcatgaacct	gctgataagc	catgttgaga	aacaaatata	tctctgacct	240
tctcatcggt	aagcagaggg	tgtaggcaac	atggaccata	gcgaanaaaa	aacttagtaa	300
tccaagctgt	tttctacact	gtaaccagggt	ttccaaccaa	ggtggaaatc	tcctatactt	360

ggtgcc

366

<210> 216
 <211> 260
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(260)
 <223> n = A,T,C or G

<400> 216
 ctgtataaac agaactccac tgcangaggg agggccgggc caggagaatc tccgcttgtc 60
 caagacaggg gcctaaggag ggtctccaca ctgctnntaa gggctnttnc atttttttat 120
 taataaaaag tnnaaaaggc ctcttctcaa cttttttccc ttnggctgga aaatttaaaa 180
 atcaaaaatt tcctnaagtt ntcaagctat catatatact ntatcctgaa aaagcaacat 240
 aattcttctt tccctccttt 260

<210> 217
 <211> 262
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(262)
 <223> n = A,T,C or G

<400> 217
 acctacgtgg gtaagtttan aaatgttata atttcaggaa naggaacgca tataattgta 60
 tcttgcttat aattttctat ttttaataagg aaatagcaaa ttgggggtggg gggaatgtag 120
 ggcattctac agtttgagca aaatgcaatt aaatgtggaa ggacagcact gaaaaatttt 180
 atgaataatc tgtatgatta tatgtctcta gagtagattt ataattagcc acttacccta 240
 atatccttca tgcttgtaaa gt 262

<210> 218
 <211> 205
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(205)
 <223> n = A,T,C or G

<400> 218
 accaaggtgg tgcattaccg gaantggatc aangacacca tctgtggcaa cccctgagca 60
 cccctatcaa ctcccttttg tagtaaaactt ggaaccttgg aaatgaccag gccaaagactc 120
 aggctcccc agttctactg acctttgtcc ttangtntna ngtcagggt tgctaggaaa 180
 anaaatcagc agacacaggt gtaaa 205

<210> 219
 <211> 114
 <212> DNA
 <213> Homo sapien

<400> 219

tactgttttg tctcagtaac aataaatata aaaagactgg ttgtgttccg gccccatcca 60
accacgaagt tgatttctct tgtgtgcaga gtgactgatt ttaaaggaca tgga 114

<210> 220
<211> 93
<212> DNA
<213> Homo sapien

<400> 220
actagccagc acaaaaggca gggtagcctg aattgctttc tgctctttac atttctttta 60
aaataagcat ttagtgctca gtccctactg agt 93

<210> 221
<211> 167
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(167)
<223> n = A,T,C or G

<400> 221
actangtgca ggtgcgcaca aatatttgtc gatattccct tcattcttga ttccatgagg 60
tcttttgccc agcctgtggc tctactgtag taagtctctg ctgatgagga gccagnatgc 120
ccccactac cttccctgac gtccccana aatcacccaa cctctgt 167

<210> 222
<211> 351
<212> DNA
<213> Homo sapien

<400> 222
agggcgtggt gcggagggcg gtactgacct cattagtagg aggatgcatt ctggcacccc 60
gttcttcacc tgtccccaa tccttaaaag gccatactgc ataaagtcaa caacagataa 120
atgtttgctg aattaaagga tggatgaaaa aaattaataa tgaatttttg cataatccaa 180
ttttctcttt tatatttcta gaagaagttt ctttgagcct attagatccc gggaaatctt 240
taggtgagca tgatttagaga gctttaggtg tgcttttaca tatatctggc atatttgagt 300
ctcgtatcaa aacaatagat tggtaaagggt ggtattattg tattgataag t 351

<210> 223
<211> 383
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(383)
<223> n = A,T,C or G

<400> 223
aaaacaaaca aacaaaaaaa acaattcttc attcagaaaa attatcttag ggactgatat 60
tggttaattat ggtaattta atwrtrttkt ggggcatttc cttacattgt cttgacaaga 120
ttaaaatgtc tgtgccaaaa ttttgatttt ttttggaga cttcttatca aaagtaatgc 180
tgccaaagga agtctaagga attagtagtg ttcccmcac ttgtttggag tgtgctattc 240
taaaagattt tgatttcctg gaatgacaat tatattttta ctttggtggg ggaaanagtt 300
ataggaccac agtcttcact tctgatactt gtaaattaat cttttattgc acttgttttg 360
accattaagc tatatgttta aaa 383

<210> 224
 <211> 320
 <212> DNA
 <213> Homo sapien

<400> 224
 cccctgaagg cttcttggtta gaaaatagta cagttacaac caataggaac aacaaaaaga 60
 aaaagtttgt gacattgtag tagggagtgt gtaccctta ctcccatca aaaaaaaat 120
 ggatacatgg ttaaaggata raagggaat attttatcat atgttctaaa agagaaggaa 180
 gagaaaatac tactttctcr aaatggaagc ccttaaaggt gctttgatac tgaaggacac 240
 aaatgtggcc gtccatcctc ctttaragtt gcatgacttg gacacggtaa ctgttgcaagt 300
 tttaractcm gcattgtgac 320

<210> 225
 <211> 1214
 <212> DNA
 <213> Homo sapien

<400> 225
 gaggactgca gcccgactc gcagccctgg caggcggcac tggatcatgga aaacgaattg 60
 ttctgctcgg gcgtcctggg gcaccccgag tgggtgctgt cagccgcaca ctgtttccag 120
 aactctaca ccacggggt gggcctgcac agtcttgagg ccgaccaaga gccagggagc 180
 cagatgggtg aggcagcct ctccgtacgg caccagagt acaacagacc cttgctcgct 240
 aacgacctca tgctcatcaa gttggacgaa tccgtgtccg agtctgacac catccggagc 300
 atcagcattg cttcgcagtg cctaccgag gggaaactct gcctcgtttc tggctggggg 360
 ctgctggcga acggcagaat gcctaccgtg ctgcagtgcg tgaacgtgtc ggtggtgtct 420
 gaggaggtct gcagtaagct ctatgacccg ctgtaccacc ccagcatgtt ctgcgccggc 480
 ggaggggaag accagaagga ctctgcaac ggtgactctg gggggccct gatctgcaac 540
 gggactctgc agggccttgt gtcttctgga aaagcccgt gtggccaagt tggcgtgcca 600
 ggtgtctaca ccaacctctg caaattcact gagtggatag agaaaaccgt ccagccaggt 660
 taactctggg gactgggaac ccatgaaatt gacccccaaa tacatcctgc ggaagggaatt 720
 caggaatatc tgttcccagc cctcctccc tcaggcccag gagtccaggc cccagcccc 780
 tcctcctca aaccaagggt acagatcccc agcccctcct ccctcagacc caggagtcca 840
 gacccccag cccctcctcc ctacagacca ggagtccagc ccctcctccc tcagaccag 900
 gagtccagac ccccgagccc ctctccctc agaccagggt gtccaggccc ccaaccctc 960
 ctccctcaga ctacaggtc caagccccc accctcctt cccagagccc agaggtccag 1020
 gtcccagccc ctctcctc agaccagcg gtccaatgcc acctagactc tcctgtaca 1080
 cagtgcctcc ttgtggcagc ttgacccaac cttaccagtt ggtttttcat ttttgtccc 1140
 tttccctag atccagaaat aaagtctaag agaagcgcaa aaaaaaaaaa aaaaaaaaaa 1200
 aaaaaaaaaa aaaa 1214

<210> 226
 <211> 119
 <212> DNA
 <213> Homo sapien

<400> 226
 acccagtatg tgcagggaga cggaacccca tgtgacagcc cactccacca gggttcccaa 60
 agaacctggc ccagtcataa tcattcatcc tgacagtggc aataatcacg ataaccagt 119

<210> 227
 <211> 818
 <212> DNA
 <213> Homo sapien

<400> 227
 acaattcata gggacgacca atgaggacag ggaatgaacc cggctctccc ccagccctga 60

tttttgctac	atatgggggtc	ccttttcatt	ctttgcaaaa	acactggggtt	ttctgagaac	120
acggacgggtt	cttagcaca	tttgtgaaat	ctgtgtaraa	ccgggctttg	caggggagat	180
aattttcctc	ctctggagga	aaggtgggtga	ttgacaggca	gggagacagt	gacaaggcta	240
gagaaagcca	cgctcgccct	tctctgaacc	aggatggaac	ggcagacccc	tgaaaacgaa	300
gcttggtccc	ttccaatcag	ccacttctga	gaacccccat	ctaacttctc	actggaaaag	360
agggctcctc	caggagcagt	ccaagagttt	tcaaagataa	cgtgacaact	accatctaga	420
ggaaaggggtg	caccctcagc	agagaagccg	agagcttaac	tctgggtcgtt	tccagagaca	480
acctgtctggc	tgtcttgagg	tgcgccagc	ctttgagagg	ccactacccc	atgaacttct	540
gccatccact	ggacatgaag	ctgaggacac	tgggcttcaa	cactgagttg	tcatgagagg	600
gacaggctct	gccctcaagc	cggctgaggg	cagcaaccac	tctcctcccc	tttctcacgc	660
aaagccattc	ccacaaatcc	agaccatacc	atgaagcaac	gagacccaaa	cagtttggct	720
caagaggata	tgaggactgt	ctcagcctgg	ctttgggctg	acaccatgca	cacacacaag	780
gtccacttct	aggttttcag	cctagatggg	agtcgtgt			818

<210> 228

<211> 744

<212> DNA

<213> Homo sapien

<400> 228

actggagaca	ctgttgaact	tgatcaagac	ccagaccacc	ccaggtctcc	ttcgtgggat	60
gtcatgacgt	ttgacatacc	tttggaaacga	gcctcctcct	tggagatgg	aagaccgtgt	120
tcgtggccga	cctggcctct	cctggcctgt	ttcttaagat	gcggagtcac	atttcaatgg	180
taggaaaagt	ggcttcgtaa	aatagaagag	cagtcactgt	ggaactacca	aatggcgaga	240
tgctcgggtg	acattggggg	gctttgggat	aaaagattta	tgagccaact	attctctggc	300
accagattct	aggccagttt	gttccactga	agcttttccc	acagcagtc	acctctgcag	360
gctggcagct	gaatggcttg	ccggtggctc	tgtggcaaga	tcacactgag	atcgatgggt	420
gagaaggcta	ggatgcttgt	ctagtgttct	tagctgtcac	gttggctcct	tccaggttgg	480
ccagacgggtg	ttggccactc	ccttctaaaa	cacaggcgcc	ctcctgggtga	cagtgacccg	540
ccgtgggatg	ccttggccca	ttccagcagt	cccagttatg	catttcaagt	ttggggtttg	600
ttcttttcgt	taatgttctc	ctgtgttgct	agctgtcttc	atttctggg	ctaagcagca	660
ttgggagatg	tggaccagag	atccactcct	taagaaccag	tggcgaaaga	cactttcttt	720
cttcactctg	aagtagctgg	tggt				744

<210> 229

<211> 300

<212> DNA

<213> Homo sapien

<400> 229

cgagtctggg	ttttgtctat	aaagtttgat	ccctcctttt	ctcatccaaa	tcagtgaac	60
cattacacat	cgaaataaaa	gaaaggtggc	agacttgccc	aacgccaggc	tgacatgtgc	120
tgcagggttg	ttgtttttta	attattattg	ttagaaacgt	caccacagct	ccctgttaat	180
ttgtatgtga	cagccaactc	tgagaaggtc	ctatttttcc	acctgcagag	gatccagtct	240
cactaggctc	ctccttgccc	tcacactgga	gtctccgcca	gtgtgggtgc	ccactgacat	300

<210> 230

<211> 301

<212> DNA

<213> Homo sapien

<400> 230

cagcagaaca	aatacaaata	tgaagagtgc	aaagatctca	taaaatctat	gctgaggaat	60
gagcgacagt	tcaaggagga	gaagcttgca	gagcagctca	agcaagctga	ggagctcagg	120
caatataaag	tcctggttca	cactcaggaa	cgagagctga	cccagttaag	ggagaagtgtg	180
cgggaaggga	gagatgcctc	cctctcattg	aatgagcatc	tccaggccct	cctcactccg	240
gatgaaccgg	acaagtccca	ggggcaggac	ctccaagaaa	cagacctcgg	ccgcgaccac	300
g						301

<210> 231
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 231
 gcaagcacgc tggcaaatct ctgtcaggtc agctccagag aagccattag tcatttttagc 60
 caggaactcc aagtccacat ccttggcaac tggggacttg cgcaggttag ccttgaggat 120
 ggcaacacgg gactttctcat caggaagtgg gatgtagatg agctgatcaa gacggccagg 180
 tctgaggatg gcaggatcaa tgatgtcagg ccggttggtg ccgccaatga tgaacacatt 240
 tttttttgtg gacatgccat ccatttctgt caggatctgg ttgatgactc ggtcagcagc 300
 c 301

<210> 232
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 232
 agtaggtatt tcgtgagaag ttcaacacca aaactggaac atagttctcc ttcaagtgtt 60
 ggcgacagcg gggcttctctg attctggaat ataactttgt gtaaattaac agccacctat 120
 agaagagtcc atctgctgtg aaggagagac agagaactct gggttccgtc gtccctgtcca 180
 cgtgctgtac caagtgtctg tgccagcctg ttacctgttc tcaactgaaaa tctggctaatt 240
 gctcttgtgt atcacttctg attctgacaa tcaatcaatc aatggcctag agcactgact 300
 g 301

<210> 233
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 233
 atgactgact tcccagtaag gctctctaag gggtaagtag gaggatccac aggatttgag 60
 atgctaaggc cccagagatc gtttgatcca accctcttat tttcagaggg gaaaatgggg 120
 cctagaagtt acagagcacc tagctgggtg gctggcacc cctggcctcac acagactccc 180
 gagtagctgg gactacaggc acacagtcac tgaagcaggc cctgttagca attctatgcg 240
 tacaaattaa catgagatga gtagagactt tattgagaaa gcaagagaaa atcctatcaa 300
 c 301

<210> 234
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 234
 aggtcctaca catcgagact catccatgat tgatatgaat ttaaaaatta caagcaaaga 60
 cattttattc atcatgatgc tttcttttgt ttcttctttt cgttttcttc tttttctttt 120
 tcaatttcag caacatactt ctcaatttct tcaggattta aaatcttgag ggattgatct 180
 cgcctcatga cagcaagttc aatgtttttg ccacctgact gaaccacttc caggagtgcc 240
 ttgatcacca gcttaatggg cagatcatct gttcaatgg cttcgtcagt atagttcttc 300
 t 301

<210> 235
 <211> 283
 <212> DNA
 <213> Homo sapien

<400> 235

tggggcgtgtg	catcaggcgg	gtttgagaaa	tattcaattc	tcagcagaag	ccagaatttg	60
aattccctca	tcttttaggg	aatcatttac	caggtttgga	gaggattcag	acagctcagg	120
tgctttcact	aatgtctctg	aacttctgtc	cctctttgtt	catggatagt	ccaataaata	180
atgttatctt	tgaactgatg	ctcataggag	agaatataag	aactctgagt	gatatcaaca	240
ttagggattc	aaagaaatat	tagatttaag	ctcacactgg	tca		283

<210> 236

<211> 301

<212> DNA

<213> Homo sapien

<400> 236

aggtcctcca	ccaactgcct	gaagcacggg	taaaattggg	aagaagtata	gtgcagcata	60
aatactttta	aatcgatcag	atttccctaa	cccacatgca	atcttcttca	ccagaagagg	120
tgggagcagc	atcattaata	ccaagcagaa	tgcgtaatag	ataaatacaa	tggtatatag	180
tgggtagacg	gcttcatgag	tacagtgtac	tgtggtatcg	taatctggac	ttgggttgta	240
aagcatcgtg	taccagtcag	aaagcatcaa	tactcgacat	gaacgaatat	aaagaacacc	300
a						301

<210> 237

<211> 301

<212> DNA

<213> Homo sapien

<400> 237

cagtggtagt	ggtggtggac	gtggcgttgg	tcgtggtgcc	ttttttggtg	cccgtcacia	60
actcaatttt	tgttcgctcc	tttttgccct	tttccaattt	gtccatctca	attttctggg	120
ccttggtctaa	tgctcatag	taggagtcct	cagaccagcc	atggggatca	aacatactct	180
ttgggtagtt	ggtgccaaag	tcgtcaatgg	cacagaatgg	atcagcttct	cgtaaatcta	240
gggttcgaa	attctttctt	cctttggata	atgtagttca	tatccattcc	ctcctttatc	300
t						301

<210> 238

<211> 301

<212> DNA

<213> Homo sapien

<400> 238

gggcagggtt	tttttttttt	ttttttgatg	gtgcagaccc	ttgctttatt	tgtctgactt	60
gttcacagtt	cagccccctg	ctcagaaaac	caacgggcca	gctaaggaga	ggaggaggca	120
ccttgagact	tccggagtcg	aggetctcca	gggttcccca	gcccataat	cattttctgc	180
acccccctgc	tggaagcag	ctccctgggg	ggtgggaatg	ggtgactaga	agggatttca	240
gtgtgggacc	cagggtctgt	tcttcacagt	aggaggtgga	agggatgact	aatttcttta	300
t						301

<210> 239

<211> 239

<212> DNA

<213> Homo sapien

<400> 239

ataagcagct	agggaattct	ttatttagta	atgtcctaac	ataaaagtcc	acataactgc	60
ttctgtcaaa	ccatgatact	gagctttgtg	acaaccaga	aataactaag	agaaggcaaa	120
cataatacct	tagagatcaa	gaaacattta	cacagttcaa	ctgtttaaaa	atagctcaac	180
attcagccag	tgagtagagt	gtgaatgcc	gcatacacag	tatacaggtc	cttcaggga	239

<210> 240

<211> 300
 <212> DNA
 <213> Homo sapien

<400> 240
 ggtcctaatag aagcagcagc ttccacattt taacgcagggt ttacggtgat actgtccttt 60
 gggatctgcc ctccagtggg accttttaag gaagaagtgg gcccaagcta agttccacat 120
 gctgggtgag ccagatgact tctgttcctt ggtcactttc ttcaatgggg cgaatggggg 180
 ctgccagggt tttaaaatca tgcttcatct tgaagcacac ggtcacttca cctcctcac 240
 gctgtgggtg tactttgatg aaaataccca ctttgttggc ctttctgaag ctataatgtc 300

<210> 241
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 241
 gaggtctggt gctgaggtct ctgggctagg aagaggaggt ctgtggagct ggaagccaga 60
 cctctttgga ggaaactcca gcagctatgt tgggtgtctct gagggaatgc aacaaggctg 120
 ctctccatg tattggaaaa ctgcaaaactg gactcaactg gaagggaagt ctgctgccag 180
 tgtgaagaac cagcctgagg tgacagaaac ggaagcaaac aggaacagcc agtcttttct 240
 tcctcctcct gtcatacggg ctctctcaag catcctttgt tgtcaggggc ctaaaaggga 300
 g 301

<210> 242
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 242
 ccgaggtcct gggatgcaac caatcactct gtttcacgtg acttttatca ccatacaatt 60
 tgtggcattt cctcattttc tacattgtag aatcaagagt gtaaataaat gtatatcgat 120
 gtcttcaaga atatatcatt cctttttcac tagaaccat tcaaaatata agtcaagaat 180
 cttaatatca acaaatatat caagcaaact ggaaggcaga ataactacca taatttagta 240
 taagtacca aagttttata aatcaaaagc cctaatagata accattttta gaattcaatc 300
 a 301

<210> 243
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 243
 aggtaagtcc cagtttgaag ctcaaaagat ctggtatgag cataggctca tcgacgacat 60
 ggtggcccaa gctatgaaat cagagggagg cttcatctgg gcctgtaaaa actatgatgg 120
 tgacgtgcag tcggactctg tggccaagg gtatggctct ctcggcatga tgaccagcgt 180
 gctggtttgt ccagatggca agacagtaga agcagaggct gccacggga ctgtaacccg 240
 tcactaccgc atgttccaga aaggacagga gacgtccacc aatcccattg cttccatttt 300
 t 301

<210> 244
 <211> 300
 <212> DNA
 <213> Homo sapien

<400> 244
 gctggtttgc aagaatgaaa tgaatgattc tacagctagg acttaacctt gaaatggaaa 60
 gtcatgcaat cccattttgca ggatctgtct gtgcacatgc ctctgtagag agcagcattc 120

ccagggacct	tggaaacagt	tgacactgta	aggtgcttgc	tccccaagac	acatccctaaa	180
aggtgttgta	atgggtgaaaa	cgtcttcctt	ctttattgcc	ccttcttatt	tatgtgaaca	240
actgtttgtc	ttttgtgtat	cttttttaaa	ctgttaaagtt	caattgtgaa	aatgaatatac	300

<210> 245
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 245						
gtctgagtat	ttaaaatggt	attgaaatta	tccccaacca	atgttagaaa	agaaagagg	60
tatatactta	gataaaaaat	gaggtgaatt	actatccatt	gaaatcatgc	tcttagaatt	120
aaggccagga	gatattgtca	ttaatgtara	cttcaggaca	ctagagtata	gcagccctat	180
gttttcaaag	agcagagatg	caattaaata	ttgttttagca	tcaaaaaggc	caactcaatac	240
agctaataaa	atgaaagacc	taattttctaa	agcaattctt	tataatttac	aaagttttaa	300
g						301

<210> 246
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 246						
ggtctgtcct	acaatgcctg	cttcttgaaa	gaagtcggca	ctttctagaa	tagctaaata	60
acctgggctt	attttaaaga	actatttgta	gctcagattg	gttttcctat	ggctaaaata	120
agtgcctctt	gtgaaaatta	aataaaacag	ttaattcaaa	gccttgatat	atgttaccac	180
taacaatcat	actaaatata	ttttgaagta	caaagtttga	catgctctaa	agtgacaacc	240
caaatgtgtc	ttacaaaaca	cgttcctaac	aaggatatgt	ttacactacc	aatgcagaaa	300
c						301

<210> 247
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 247						
aggtcctttg	gcagggctca	tggatcagag	ctcaaactgg	agggaaaggc	atttcgggta	60
gcctaagagg	gcgactggcg	gcagcacaac	caaggaaggc	aaggttgttt	ccccacgct	120
gtgtcctgtg	ttcaggtgcg	acacacaatc	ctcatgggaa	caggatcacc	catgcgctgc	180
ccttgatgat	caaggttggg	gcttaagtgg	attaagggag	gcaagttctg	ggttccttgc	240
cttttcaaac	catgaagtca	ggctctgtat	ccctcctttt	cctaactgat	attctaacta	300
a						301

<210> 248
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 248						
aggtccttgg	agatgccatt	tcagccgaag	gactcttctw	ttcggaagta	caccctcact	60
attaggaaga	ttcttagggg	taatttttct	gaggaaggag	aactagccaa	cttaagaatt	120
acaggaagaa	agtggtttgg	aagacagcca	aagaaataaa	agcagattaa	attgtatcag	180
gtacattcca	gcctgttggc	aactccataa	aaacatttca	gatttttaac	ccgaatttag	240
ctaattgagac	tggatttttg	ttttttatgt	tgtgtgtcgc	agagctaaaa	actcagttcc	300
c						301

<210> 249
 <211> 301

<212> DNA

<213> Homo sapien

<400> 249

```

gtccagagga agcacctggg gctgaactag gcttgccctg ctgtgaactt gcacttggag      60
ccctgacgct gctgttctcc ccgaaaaacc cgaccgacct ccgcgatctc cgtcccgccc      120
ccagggagac acagcagtga ctgagagctg gtgcacacct gtgcctccct cctcaccgcc      180
catcgtaatg aattattttg aaaattaatt ccaccatcct ttcagattct ggatggaaag      240
actgaatctt tgactcagaa ttgtttgctg aaaagaatga tgtgactttc ttagtcattt      300
a                                                                                   301

```

<210> 250

<211> 301

<212> DNA

<213> Homo sapien

<400> 250

```

ggtctgtgac aaggacttgc aggctgtggg aggcaagtga cccttaacac tacactttct      60
cttatcttta ttggcttgat aaacataatt atttctaaca ctagcttatt tccagttgcc      120
cataagcaca tcagtacttt tctctggctg gaatagtaaa ctaaagtatg gtacatctac      180
ctaaaagact actatgtgga ataatacata ctaatgaagt attacatgat ttaaagacta      240
caataaaacc aaacatgctt ataacattaa gaaaaacaat aaagatacat gattgaaacc      300
a                                                                                   301

```

<210> 251

<211> 301

<212> DNA

<213> Homo sapien

<400> 251

```

gccgaggtcc tacatttggc ccagtttccc cctgcacact ctccagggcc cctgcctcat      60
agacaacctc atagagcata ggagaactgg ttgccctggg ggcaggggga ctgtctggat      120
ggcaggggtc ctcaaaaatg ccactgtcac tgccaggaaa tgcttctgag cagtacacct      180
cattgggatc aatgaaaagc ttcaagaaat cttcaggctc actctcttga aggcccgga      240
cctctggagg ggggcagtgg aatcccagct ccaggacgga tcctgtcgaa aagatatacct      300
c                                                                                   301

```

<210> 252

<211> 301

<212> DNA

<213> Homo sapien

<400> 252

```

gcaaccaatc actctgtttc acgtgacttt tatcaccata caatttgtgg catttcctca      60
ttttctacat tgtagaatca agagtgtaaa taaatgtata tcgatgtctt caagaatata      120
tcatttcctt ttacttagga acccattcaa aatataagtc aagaatctta atatcaacaa      180
atatatcaag caaactggaa ggcagaataa ctaccataat ttagtataag taccctaaagt      240
tttataaatc aaaagcccta atgataacca tttttagaat tcaatcatca ctgtagaate      300
a                                                                                   301

```

<210> 253

<211> 301

<212> DNA

<213> Homo sapien

<400> 253

```

ttccctaaga agatgttatt ttgttgggtt ttgttcccc tccatctcga ttctcgtacc      60
caactaaaaa aaaaaaataa agaaaaaatg tgctgcgttc tgaaaaataa ctcttagct      120

```

```

tggtctgatt gttttcagac cttaaaatat aaacttggtt cacaagcttt aatccatgtg      180
gatttttttt cttagagaac cacaaaacat aaaaggagca agtcggactg aatacctgtt      240
tccatagtgc ccacagggtg ttcctcacat tttctccata ggaaaatgct ttttccaag      300
g                                                                 301

```

```

<210> 254
<211> 301
<212> DNA
<213> Homo sapien

```

```

<400> 254
cgctgcgcct ttcccttggg ggaggggcaa ggccagaggg ggtccaagtg cagcacgagg      60
aacttgacca attcccttga agcgggtggg ttaaaccctg taaatgggaa caaaatcccc      120
ccaaatctct tcatcttacc ctggtggact cctgactgta gaattttttg gttgaaacaa      180
gaaaaaaata aagcttttga cttttcaagg ttgcttaaca ggtactgaaa gactggcctc      240
acttaaaactg agccaggaaa agctgcagat ttattaatgg gtgtgttagt gtgcagtgcc      300
t                                                                 301

```

```

<210> 255
<211> 302
<212> DNA
<213> Homo sapien

```

```

<400> 255
agcttttttt tttttttttt tttttttttt ttcattaaaa aatagtgtct tttattataa      60
attactgaaa tgtttctttt ctgaatataa atataaatat gtgcaaagtt tgacttggat      120
tggtattttg ttgagttctt caagcatctc ctaataccct caagggcctg agtagggggg      180
aggaaaaagg actggagggtg gaatctttat aaaaaacaag agtgattgag gcagattgta      240
aacattatta aaaaacaaga aacaaacaaa aaaatagaga aaaaaaccac cccaacacac      300
aa                                                                 302

```

```

<210> 256
<211> 301
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(301)
<223> n = A,T,C or G

```

```

<400> 256
gttccagaaa acattgaagg tggcttccca aagtctaact agggataccc cctctagcct      60
aggacctctc tcccacacc tcaatccacc aaaccatcca taatgcaccc agataggccc      120
acccccaaaa gcctggacac cttgagcaca cagttatgac caggacagac tcatctctat      180
aggcaaatag ctgctggcaa actggcatta cctggtttgt ggggatgggg gggcaagtgt      240
gtggcctctc ggctgggtta gcaagaacat tcagggtagg cctaagttn tctgtttagt      300
t                                                                 301

```

```

<210> 257
<211> 301
<212> DNA
<213> Homo sapien

```

```

<400> 257
gttggtggagg aactctggct tgctcattaa gtcctactga ttttactat cccctgaatt      60
tccccactta tttttgtctt tcaatctgc aggccttaga agaggtctac ctgcctccag      120
tcttacctag tccagtctac cccctggagt tagaatggcc atcctgaagt gaaaagtaat      180

```

```

gtcacattac tcccttcagt gatttcttgt agaagtgcc atccctgaat gccaccaaga 240
tcttaatctt cacatcttta atcttatctc tttgactcct ctttacaccg gagaaggctc 300
c 301

```

```

<210> 258
<211> 301
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(301)
<223> n = A,T,C or G

```

```

<400> 258
cagcagtagt agatgccgta tgccagcacg cccagcactc ccaggatcag caccagcacc 60
aggggcccag ccaccaggcg cagaagcaag ataaacagta ggctcaagac cagagccacc 120
cccaggggcaa caagaatcca ataccaggac tgggcaaaat cttcaaagat ctttaacctg 180
atgtctcggg cattgaggct gtcaataana cgctgatccc ctgctgtatg gtggtgtcat 240
tggtgatccc tgggagcgcc ggtggagtaa cgttggtcca tggaaagcag cgcccacaac 300
t 301

```

```

<210> 259
<211> 301
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(301)
<223> n = A,T,C or G

```

```

<400> 259
tcatatatgc aaacaaatgc agactangcc tcaggcagag actaaaggac atctcttggg 60
gtgtcctgaa gtgatttgga cccctgaggg cagacacctc agtaggaatc ccagtgggaa 120
gcaaagccat aaggaagccc aggattcctt gtgatcagga agtgggcccag gaaggtctgt 180
tccagctcac atctcatctg catgcagcac ggaccggatg cgcccaactg gtcttggctt 240
ccctcccatc ttctcaagca gtgtccttgt tgagccattt gcaccccttg ctccagggtg 300
c 301

```

```

<210> 260
<211> 301
<212> DNA
<213> Homo sapien

```

```

<400> 260
tttttttct ccctaaggaa aaagaaggaa caagtctcat aaaaccaa at aagcaatgg 60
aaggtgtctt aacttgaaaa agattaggag tcaactgggtt acaagttata attgaatgaa 120
agaactgtaa cagccacagt tggccatttc atgccaatgg cagcaaaca caggattaac 180
tagggcaaaa taaataagtg tgtggaagcc ctgataagtg ctttaataaac agactgattc 240
actgagacat cagtacctgc ccgggcggcc gctcgagccg aattctgcag atatccatca 300
c 301

```

```

<210> 261
<211> 301
<212> DNA
<213> Homo sapien

```

<400> 261

```

aaatattcga gcaaatcctg taactaatgt gtctccataa aaggctttga actcagtgaa    60
tctgcttcca tccacgattc tagcaatgac ctctcggaca tcaaagctcc tcttaagggtt    120
agcaccaact attccataca attcatcagc aggaaataaa ggctcttcag aagggttcaat    180
ggtgacatcc aatttcttct gataatttag attcctcaca accttcctag ttaagtgaag    240
ggcatgatga tcatccaaag ccagtggtc atttactcca gactttctgc aatgaagatc    300
a                                                                    301

```

<210> 262

<211> 301

<212> DNA

<213> Homo sapien

<400> 262

```

gaggagagcc tggtacagca tttgtaagca cagaatactc caggagtatt tgtaattgtc    60
tgtgagcttc ttgccgcaag tctctcagaa atttaaaaag atgcaaatcc ctgagtcacc    120
cctagacttc ctaaacacaga tcctctgggg ctggaacctg gcactctgca tttgtaatga    180
gggctttctg gtgcacacct aattttgtgc atctttgccc taaatcctgg attagtgcc    240
catcattacc cccacattat aatgggatag attcagagca gatactctcc agcaaagaat    300
c                                                                    301

```

<210> 263

<211> 301

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (301)

<223> n = A,T,C or G

<400> 263

```

tttagcttgt ggtaaatgac tcacaaaact gattttaaaa tcaagttaat gtgaattttg    60
aaaattacta cttaatccta attcacaata acaatggcat taaggtttga cttgagttgg    120
ttcttagtat tatttatggg aaataggctc ttaccacttg caaataactg gccacatcat    180
taatgactga cttcccagta aggctctcta aggggtaagt angaggatcc acaggatttg    240
agatgctaag gcccagaga tcgtttgatc caaccctctt attttcagag gggaaaatgg    300
g                                                                    301

```

<210> 264

<211> 301

<212> DNA

<213> Homo sapien

<400> 264

```

aaagacgtta aaccactcta ctaccacttg tggaactctc aaagggtaaa tgacaaaacc    60
aatgaatgac tctaaaaaca atatttacat ttaatggttt gtagacaata aaaaaacaag    120
gtggatagat ctagaattgt aacattttta gaaaaccata scatttgaca gatgagaaag    180
ctcaattata gatgcaaagt tataactaaa ctactatagt agtaaagaaa tacatttcac    240
acccttcata taaattcact atcttggtt gaggcactcc ataaaatgta tcacgtgcat    300
a                                                                    301

```

<210> 265

<211> 301

<212> DNA

<213> Homo sapien

<400> 265

tgcccaagtt atgtgtaagt gtatccgcac ccagaggtaa aactacactg tcattctttgt	60
cttcttggtga cgcagtatctt cttctctggg gagaagccgg gaagtcttct cctggctcta	120
catattcttg gaagtctcta atcaactttt gttccatttg tttcatttct tcaggaggga	180
tttccagttt gtcaacatgt tctctaacaa cacttgccca tttctgtaaa gaatccaaag	240
cagtccaagg ctttgacatg tcaacaacca gcataactag agtatccttc agagatacgg	300
c	301

<210> 266
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 266	
taccgtctgc ctttctccc atccaggcca tctgcgaatc tacatgggtc ctcctattcg	60
acaccagatc actctttcct ctaccacag gcttgctatg agcaagagac acaacctcct	120
ctcttctgtg ttccagcttc ttttctgtt ctccccccc ctttaagttct attcctgggg	180
atagagacac caatacccat aacctctctc ctaagcctcc ttataacca ggggtgcacag	240
cacagactcc tgacaactgg taaggccaat gaactgggag ctcacagctg gctgtgcctg	300
a	301

<210> 267
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 267	
aaagagcaca ggccagctca gcctgccctg gccatctaga ctcagcctgg ctccatgggg	60
gttctcagtg ctgagtccat ccaggaaaag ctcacctaga cttctctgagg ctgaatcttc	120
atcctcacag gcagcttctg agagcctgat attcctagcc ttgatgggtc ggagtaaagc	180
ctcattctga ttcctctcct tcttttcttt caagttggct ttcctcacat cctctgttc	240
aattcgcttc agcttgtctg ctttagccct catttccaga agcttcttct ctttggcatt	300
t	301

<210> 268
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 268	
aatgtctcac tcaactactt cccagcctac cgtggcctaa ttctgggagt tttcttctta	60
gatcttgga gagctggttc ttctaaggag aaggaggaag gacagatgta actttggatc	120
tcgaagagga agtctaattg aagtaattag tcaacgggtc ttgttttagac tcttggata	180
tgctgggtgg ctcaagtggc ctttttgga aaagcaagta ttattcttaa ggagtaacca	240
cttcccattg ttctactttc taccatcatc aattgtatat tatgtattct ttggagaact	300
a	301

<210> 269
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 269	
taacaatata cactagctat ctttttaact gtccatcatt agcaccaatg aagattcaat	60
aaaattacct ttattcacac atctcaaac aattctgcaa attcttagtg aagtttaact	120
atagtcacag accttaata ttacattgt tttctatgtc tactgaaaat aagttcacta	180
cttttctgga tattctttac aaaatcttat taaaattcct ggtattatca ccccaatta	240
tacagtagca caaccacctt atgtagtttt tacatgatag ctctgtagaa gtttcacatc	300
t	301

<210> 270
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 270
 cattgaagag cttttgogaa acatcagaac acaagtgcctt ataaaattaa ttaagcctta 60
 cacaagaata catattcctt ttattttctaa ggagttaaac atagatgtag ctgatgtgga 120
 gagcttgctg gtgcagtgca tattggataa cactattcat ggccgaattg atcaagtcaa 180
 ccaactcctt gaactggatc atcagaagaa ggggtggtgca cgatatactg cactagataa 240
 tggaccaacc aactaaattc tctcaccagg ctgtatcagt aaactggcctt aacagaaaac 300
 a 301

<210> 271
 <211> 301
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1) ... (301)
 <223> n = A,T,C or G

<400> 271
 aaaagggttct cataagatta acaatttaaa taaatatttg atagaacatt ctttctcatt 60
 tttatagctc atcttttaggg ttgatattca gttcatgctt cccttgctgt tcttgatcca 120
 gaattgcaat cacttcatca gcctgtattc gctccaattc tctataaagt ggggtccaagg 180
 tgaaccacag agccacagca cacctctttc ccttggtgac tgccttcacc ccatganggt 240
 tctctcctcc agatganaac tgatcatgcy cccacatttt gggttttata gaagcagtca 300
 c 301

<210> 272
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 272
 taaattgcta agccacagat aacaccaatc aaatggaaca aatcactgtc ttcaaagtgc 60
 ttatcagaaa accaaatgag cctggaatct tcataatacc taaacatgcc gtatttagga 120
 tccaataatt ccctcatgat gagcaagaaa aattctttgc gcacctctcc tgcattccaca 180
 gcatcttctc caacaaatat aaccttgagt ggcttcttgt aatctatgtt ctttgttttc 240
 ctaaggactt ccattgcac tcctacaata ttttctctac gcaccactag aattaagcag 300
 g 301

<210> 273
 <211> 301
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1) ... (301)
 <223> n = A,T,C or G

<400> 273
 acatgtgtgt atgtgtatct ttgggaaaaa aanaagacat cttgtttayt atttttttgg 60
 agagangctg ggacatggat aatcacwtaa tttgtayta tyactttaat ctgactyga 120

```

gaaccgtcta aaaataaaat ttaccatgtc dtatattcct tatagtatgc ttatttcacc 180
ttytttctgt ccagagagag tatcagtgac ananatttma ggggtgaamac atgmattggg 240
gggacttnty ttacngagm accctgcccg sgcgcctcg makngantt ccgcsananc 300
t 301

```

```

<210> 274
<211> 301
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(301)
<223> n = A,T,C or G

```

```

<400> 274
cttatatact ctttctcaga ggcaaaagag gagatgggta atgtagacaa ttctttgagg 60
aacagtaaat gattattaga gagaangaat ggaccaagga gacagaaatt aacttgtaaa 120
tgattctctt tggaatctga atgagatcaa gaggccagct ttagcttggt gaaaagtcca 180
tctaggtatg gttgcattct cgtcttctt tctgcagtag ataatgaggt aaccgaaggc 240
aattgtgctt cttttgataa gaagctttct tggtcatatc aggaaattcc aganaaagtc 300
c 301

```

```

<210> 275
<211> 301
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(301)
<223> n = A,T,C or G

```

```

<400> 275
tcggtgtcag cagcacgtgg cattgaacat tgcaatgtgg agcccaaacc acagaaaatg 60
gggtgaaatt ggccaacttt ctattaactt atgttggcaa ttttgccacc aacagtaagc 120
tggcccttct aataaaagaa aattgaaagg tttctcacta aacggaatta agtagtgag 180
tcaagagact ccagggcctc agcgtacctg cccggggcggc cgctcgaagc cgaattctgc 240
agatatccat cacactggcg gncgctcgan catgcatcta gaaggnccaa ttcgccctat 300
a 301

```

```

<210> 276
<211> 301
<212> DNA
<213> Homo sapien

```

```

<400> 276
tgtacacata ctcaataaat aaatgactgc attgtggtat tattactata ctgattatat 60
ttatcatgtg acttctaatt agaaaaatgta tccaaaagca aaacagcaga tatacaaaat 120
taaagagaca gaagatagac attaacagat aaggcaactt atacattgag aatccaaatc 180
caatacatth aaacattttg gaaatgaggg ggacaaatgg aagccagatc aaatttgtgt 240
aaaactattc agtatgtttc ctttgcttca tgtctgagaa ggctctcctt caatggggat 300
g 301

```

```

<210> 277
<211> 301
<212> DNA
<213> Homo sapien

```

<220>
 <221> misc_feature
 <222> (1)...(301)
 <223> n = A,T,C or G

<400> 277
 tttgttgatg tcagtatttt attacttgcg ttatgagtgc tcacctggga aattctaaag 60
 atacagagga cttggaggaa gcagagcaac tgaattttaat ttaaaagaag gaaaacattg 120
 gaatcatggc actcctgata ctttcccaaa tcaacactct caatgcccc cctcgtcct 180
 caccatagtg gggagactaa agtggccacg gatttgccct angtgtgcag tgcgttctga 240
 gttcncgtgc gattacatct gaccagtctc ctttttccga agtcntccg ttcaatcttg 300
 c 301

<210> 278
 <211> 301
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(301)
 <223> n = A,T,C or G

<400> 278
 taccactaca ctccagcctg ggcaacagag caagacctgt ctcaaagcat aaaatggaat 60
 aacatatcaa atgaaacagg gaaaatgaag ctgacaattt atggaagcca gggcttgtca 120
 cagtctctac tgttattatg cattacctgg gaatttatat aagcccttaa taataatgcc 180
 aatgaacatc tcatgtgtgc tcacaatgtt ctggcactat tataagtgtc tcacaggttt 240
 tatgtgttct tcgtaacttt atggantagg tactcggccg cgaacacgct aagccgaatt 300
 c 301

<210> 279
 <211> 301
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(301)
 <223> n = A,T,C or G

<400> 279
 aaagcaggaa tgacaaagct tgcttttctg gtatgttcta ggtgtattgt gacttttact 60
 gttatattaa ttgccaatat aagtaaatat agattatata tgtatagtgt ttcacaaagc 120
 ttagaccttt accttccagc caccacacag tgcttgatat ttcagagtca gtcattgggt 180
 atacatgtgt agttccaaag cacataagct agaanaanaa atatttctag ggagcactac 240
 catctgtttt cacatgaaat gccacacaca tagaactcca acatcaattt cattgcacag 300
 a 301

<210> 280
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 280
 ggtactggag ttttctccc ctgtgaaaac gtaactactg ttgggagtga attgaggatg 60
 tagaaaggtg gtggaaccaa attgtggtca atggaaatag gagaatatgg ttctcactct 120

tgagaaaaaa acctaagatt agcccaggtg gttgcctgta acttcagttt ttctgcctgg	180
gtttgatata gtttaggggt ggggttagat taagatctaa attacatcag gacaaagaga	240
cagactatta actccacagt taattaagga ggtatgttcc atgtttattt gttaaagcag	300
t	301

<210> 281
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 281	
aggtacaaga aggggaatgg gaaagagctg ctgctgtggc attgttcaac ttggatattc	60
gccgagcaat ccaaatcctg aatgaagggg catcttctga aaaaggagat ctgaatctca	120
atgtggtagc aatggcttta tcgggttata cggatgagaa gaactccctt tggagagaaa	180
tgtgtagcac actgcgatta cagctaaata acccgatatt gtgtgtcatg ttgcatcttc	240
tgacaagtga aacaggatct tacgatggag ttttgtatga aaacaaagtt gcagtacctc	300
g	301

<210> 282
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 282	
caggtactac agaattaataa tactgacaag caagtagttt cttggcgtgc acgaattgca	60
tccagaaccc aaaaattaag aaattcaaaa agacattttg tgggcacctg ctagcacaga	120
agcgacagag caaagcccag gcagaacat gctaacctta cagctcagcc tgcacagaag	180
cgcagaagca aagcccaggc agaaccatgc taaccttaca gctcagcctg cacagaagcg	240
cagaagcaaa gccccaggcag aacatgctaa ccttaacagct cagcctgcac agaagcacag	300
a	301

<210> 283
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 283	
atctgtatac ggcagacaaa ctttatarag tgtagagagg tgagcgaag gatgcaaaag	60
cactttgagg gctttataat aatatgctgc ttgaaaaaaa aaatgtgtag ttgatactca	120
gtgcatctcc agacatagta aggggttgct ctgaccaatc aggtgatcat tttttctatc	180
acttcccagg ttttatgcaa aaattttgtt aaattctata atggtgatat gcattcttta	240
ggaaacatat acatttttaa aaatctattt tatgtaagaa ctgacagacg aatttgcttt	300
g	301

<210> 284
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 284	
caggtacaaa acgctattaa gtggcttaga atttgaacat ttgtggtctt tatttacttt	60
gcttcgtgtg tgggcaaagc aacatcttcc ctaaatatat attaccaaga aaagcaagaa	120
gcagattagg tttttgacaa aacaaacagg ccaaaaaggg gctgacctgg agcagagcat	180
ggtgagaggc aaggcatgag agggcaagtt tgttgtggac agatctgtgc ctactttatt	240
actggagtaa aagaaaacaa agttcattga tgtcgaagga tatatacagt gttagaaatt	300
a	301

<210> 285

<211> 301
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(301)
 <223> n = A,T,C or G

<400> 285
 acatcaccat gatcggtatcc cccacccatt atacgttgta tgtttacata aatactcttc 60
 aatgatcatt agtgttttaa aaaaaatact gaaaactcct tctgcatccc aatctctaac 120
 caggaaagca aatgctatctt acagacctgc aagccctccc tcaaacnaaa ctatttctgg 180
 attaaatag tctgacttct tttgaggtca cagcactagg caaatgctat ttacgatctg 240
 caaaagctgt ttgaagagtc aaagcccca tgtgaacacg atttctggac cctgtaacag 300
 t 301

<210> 286
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 286
 taccactgca ttccagcctg ggtgacagag tgagactccg tctccaaaa aaactttgct 60
 tgtatattat ttttgctta cagtggatca ttctagtagg aaaggacagt aagatttttt 120
 atcaaaatgt gtcatgccag taagagatgt tatattcttt tctcatttct tccccacca 180
 aaaataagct accatatagc ttataagtct caaatttttg ccttttacta aaatgtgatt 240
 gtttctgttc attgtgtatg cttcatcacc tatattaggc aaattccatt tttcccttg 300
 t 301

<210> 287
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 287
 tacagatctg ggaactaaat attaaaaatg agtgtggctg gatatatgga gaatgttggg 60
 ccagaagga acgtagagat cagatattac aacagctttg ttttgagggg tagaaatatg 120
 aaatgatttg gttatgaacg cacagttagg gcagcagggc cagaatcctg accctctgcc 180
 ccgtggttat ctctcccca gcttggtgc ctcagtgtat cacagtattc cattttgttt 240
 gttgcatgtc ttgtgaagcc atcaagattt tctcgtctgt tttcctctca ttggtaatgc 300
 t 301

<210> 288
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 288
 gtacacctaa ctgcaaggac agctgaggaa tgtaatgggc agccgctttt aaagaagtag 60
 agtcaatagg aagacaaatt ccagttccag ctcagtctgg gtatctgcaa agctgcaaaa 120
 gatctttaaa gacaatttca agagaatatt tccttaaagt tggcaatttg gagatcatac 180
 aaaagcatct gcttttgtga ttttaatttag ctcactctggc cactggaaga atccaaacag 240
 tctgccttaa ttttggatga atgcatgatg gaaattcaat aatttagaaa gttaaaaaaa 300
 a 301

<210> 289
 <211> 301

<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)... (301)
<223> n = A,T,C or G

<400> 289
ggtacactgt ttccatgtta tgtttctaca cattgctacc tcagtgtccc tggaaactta . 60
gcttttgatg tctccaagta gtccaccttc atttaactct ttgaaactgt atcatctttg 120
ccaagtaaga gtggtggcct atttcagctg ctttgacaaa atgactggct cctgacttaa 180
cgttctataa atgaatgtgc tgaagcaaag tgcccatggg ggcggcgaan aagagaaaga 240
tgtgttttgt tttggactct ctgtgggtccc ttccaatgct gtgggtttcc aaccagnnga 300
a 301

<210> 290
<211> 301
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)... (301)
<223> n = A,T,C or G

<400> 290
acactgagct cttcttgata aatatacaga atgcttggca tatacaagat tctatactac . 60
tgactgatct gttcatttct ctccacagctc ttaccccaaa aagcttttcc accctaagtg 120
ttctgacctc cttttctaata cacagtaggg atagaggcag anccacctac aatgaacatg 180
gagttctatc aagaggcaga aacagcacag aatcccagtt ttaccattcg ctgacagtgc 240
tgccttgaac aaaaacattt ctccatgtct cattttcttc atgcctcaag taacagtgag 300
a 301

<210> 291
<211> 301
<212> DNA
<213> Homo sapien

<400> 291
caggtaccaaa tttcttctat cctagaaaca ttccatttta tggtgttgaa acataacaac . 60
tatatcagct agattttttt tctatgcttt acctgctatg gaaaatttga cacattctgc 120
tttactcttt tgtttatagg tgaatcaciaa aatgtatttt tatgtattct gtagttcaat 180
agccatggct gtttacttca tttaatttat ttagcataaa gacattatga aaaggcctaa 240
acatgagctt cacttccccca ctaactaatt agcatctggt atttcttaac cgtaatgcct 300
a 301

<210> 292
<211> 301
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)... (301)
<223> n = A,T,C or G

<400> 292

```

accttttagt agtaatgtct aataataaat aagaaatcaa ttttataagg tccatatagc      60
tgtattaaat aatttttaag tttaaaagat aaaataccat cattttaaat gttggtattc      120
aaaaccaaag natataaccg aaaggaaaaa cagatgagac ataaaatgat ttgcnagatg      180
ggaaatatag tasttyatga atgttnatta aattccagtt ataatagtgg ctacacactc      240
tcactacaca cacagacccc acagtcctat atgccacaaa cacatttcca taacttgaaa      300
a                                                                    301

```

```

<210> 293
<211> 301
<212> DNA
<213> Homo sapien

```

```

<400> 293
ggtaccaagt gctgggtgcc gctgtgtacc tgttctcact gaaaagtctg gctaagtctc      60
ttgtgtagtc acttctgatt ctgacaatca atcaatcaat ggccatagagc actgactggt      120
aacacaaacg tcactagcaa agtagcaaca gctttaagtc taaatacaaaa gctgttctgt      180
gtgagaattt tttaaaaggc tacttgtata ataacccttg tcatttttaa tgtacctcgg      240
ccgcgaccac gctaagccga attctgcaga tatccatcac actggcgggc gctcgagcat      300
g                                                                    301

```

```

<210> 294
<211> 301
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(301)
<223> n = A,T,C or G

```

```

<400> 294
tgacccataa caatatacac tagctatctt tttaaactgtc catcattagc accaatgaag      60
attcaataaa attaccttta ttcacacatc tcaaaacaat tctgcaaatt cttagtgaag      120
tttaactata gtcacaganc ttaaataatc acattgtttt ctatgtctac tgaaaataag      180
ttcactactt ttctgggata ttctttacaa aatcttatta aaattcctgg tattatcacc      240
cccaattata cagtagcaca accaccttat gtagttttta catgatagct ctgtagaggt      300
t                                                                    301

```

```

<210> 295
<211> 305
<212> DNA
<213> Homo sapien

```

```

<400> 295
gtactctttc tctcccctcc tctgaattta attctttcaa cttgcaattt gcaaggatta      60
cacatttcac tgtgatgtat attgtgttgc aaaaaaaaaa gtgtctttgt ttaaaattac      120
ttggtttgtg aatccatctt gctttttccc cattggaact agtcattaac ccattctctga      180
actggtagaa aaacrtctga agagctagtc tatcagcatc tgacagggtga attggatggt      240
tctcagaacc atttcacca gacagcctgt ttctatcctg ttttaataaat tagtttgggg      300
tctct                                                                    305

```

```

<210> 296
<211> 301
<212> DNA
<213> Homo sapien

```

```

<400> 296
aggtactatg ggaagctgct aaaataatat ttgatagtaa aagtatgtaa tgtgctatct      60

```

```

cacctagtag taaactaaaa ataaactgaa actttatgga atctgaagtt attttccttg 120
attaataga attaataaac caatatgagg aaacatgaaa ccatgcaatc tactatcaac 180
tttgaaaaag tgattgaacg aaccacttag ctttcagatg atgaacactg ataagtcatt 240
tgtcattact ataaatttta aaatctgtta ataagatggc ctatagggag gaaaaagggg 300
c 301

```

```

<210> 297
<211> 300
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(300)
<223> n = A,T,C or G

```

```

<400> 297
actgagtttt aactggacgc caagcaggca aggctggaag gttttgctct ctttggtgcta 60
aaggttttga aaaccttgaa ggagaatcat ttgacaaga agtacttaag agtctagaga 120
acaaagangt gaaccagctg aaagctctcg ggggaanctt acatgtgttg ttaggcctgt 180
tccatcattg ggagtgcact ggccatccct caaaatttgt ctgggctggc ctgagtgggc 240
accgcacctc ggccgcgacc acgctaagcc gaattctgca gatatccatc acactggcgg 300

```

```

<210> 298
<211> 301
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(301)
<223> n = A,T,C or G

```

```

<400> 298
tatgggggttt gtcacccaaa agctgatgct gagaaaggcc tccctggggc ccctcccgcg 60
ggcatctgag agacctggtg ttccagtgtt tctggaaatg ggtcccagtg ccgccggctg 120
tgaagctctc agatcaatca cgggaagggc ctggcggtgg tggccacctg gaaccaccct 180
gtcctgtctg ttacatttc actaycaggt tttctctggg cattacnatt tgttccccta 240
caacagtgac ctgtgcatte tgctgtggcc tgctgtgtct gcagggtggc ctcagcgagg 300
t 301

```

```

<210> 299
<211> 301
<212> DNA
<213> Homo sapien

```

```

<400> 299
gttttgagac ggagtttcac tcttgttgcc cagactggac tgcaatggca gggctctctgc 60
tcactgcacc ctctgcctcc caggttcgag caattctcct gcctcagcct cccaggtagc 120
tgggattgca ggctcacgcc accataccca gctaattttt ttgtattttt agtagagacg 180
gagtttcgcc atgttggcc aactcctgac ctcaagcgac ctgcctgcct 240
cggcctccca aagtgtcgga attataggca tgagtcaaca cgcccagcct aaagatatatt 300
t 301

```

```

<210> 300
<211> 301
<212> DNA
<213> Homo sapien

```

<400> 300
 attcagtttt atttgctgcc ccagtatctg taaccaggag tgccacaaaa tcttgccaga 60
 tatgtccac acccactggg aaaggctccc acctggctac ttctctatc agctgggtca 120
 gctgcattcc acaagggtct cagcctaag agtttacta cctgccagtc tcaaaactta 180
 gtaaagcaag accatgacat tccccacgg aaatcagagt ttgccccacc gtcttgttac 240
 tataaagcct gcctctaaca gtccttgctt cttcacacca atcccgagcg catccccat 300
 g 301

<210> 301
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 301
 ttaaattttt gagaggataa aaaggacaaa taatctagaa atgtgtcttc ttcagtctgc 60
 agaggacccc aggtctccaa gcaaccacat ggtcaagggc atgaataatt aaaagtgggt 120
 gggaactcac aaagaccctc agagctgaga caccacaac agtgggagct cacaaagacc 180
 ctgagagctg agacacccac aacagtggga gctcacaag accctcagag ctgagacacc 240
 cacaacagca cctcgttcag ctgccacatg tgtgaataag gatgcaatgt ccagaagtgt 300
 t 301

<210> 302
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 302
 aggtacacat ttagcttgtg gtaaatgact cacaaaactg attttaaaat caagttaatg 60
 tgaattttga aaattactac ttaatcctaa ttcacaataa caatggcatt aaggtttgac 120
 ttgagttggt tcttagtatt atttatggta aataggctct taccacttgc aaataactgg 180
 ccacatcatt aatgactgac ttcccagtaa ggctctctaa ggggtaagta ggaggatcca 240
 caggatttga gatgctaagg ccccagagat cgtttgatcc aaccctctta ttttcagagg 300
 g 301

<210> 303
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 303
 aggtaccaac tgtggaaata ggtagaggat cattttttct ttccatatca actaagtgtg 60
 atattgtttt ttgacagttt aacacatctt cttctgtcag agattcttct acaatagcac 120
 tggctaattg aactaccgct tgcattgtaa aaatgggtgg ttgtgaaatg atcataggcc 180
 agtaacgggt atgtttttct aactgatctt ttgctcgttc caaagggacc tcaagacttc 240
 catcgatttt atatctgggg tctagaaaag gagttaatct gttttccctc ataaattcac 300
 c 301

<210> 304
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 304
 acatggatgt tatttttcag actgtcaacc tgaatttgta tttgcttgac attgcctaatt 60
 tattagtctt agtttcagct taccactttt ttgtctgcaa catgcaraas agacagtgcc 120
 ctttttagtg tatcatatca ggaatcatct cacattgggt ttgtgccatta ctggtgcagt 180
 gactttcagc cacttgggta aggtggagtt ggccatatgt ctccactgca aaattactga 240

ttttcctttt gtaattaata agtgtgtgtg tgaagattct ttgagatgag gtatatatct 300
c 301

<210> 305
<211> 301
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(301)
<223> n = A,T,C or G

<400> 305
gangtacagc gtggtcaagg taacaagaag aaaaaaatgt gagtggcatc ctgggatgag 60
cagggggaca gacctggaca gacacgttgt catttgctgc tgtgggtagg aaaatgggag 120
taaaggagga gaaacagata caaaatctcc aactcagtat taaggatttc tcatgcctag 180
aatattggta gaaacaagaa tacattcata tggcaaataa ctaaccatgg tggaacaaaa 240
ttctgggatt taagtggat accaangaaa ttgtattaaa agagctgttc atggaataag 300
a 301

<210> 306
<211> 8
<212> PRT
<213> Homo sapien

<400> 306
Val Leu Gly Trp Val Ala Glu Leu
1 5

<210> 307
<211> 637
<212> DNA
<213> Homo sapien

<400> 307
acagggratg aagggaagg gagaggatga ggaagccccc ctggggattt ggtttgggtcc 60
tttgtatcag gtggtctatg gggcttatcc ctacaaagaa gaatccagaa atagggggcac 120
attgaggaat gatacttgag cccaaagagc attcaatcat tgttttattt gccttmtttt 180
cacaccattg gtgagggagg gattaccacc ctggggttat gaagatgggt gaacacccca 240
cacatagcac cggagatatg agatcaacag tttcttagcc atagagattc acagcccaga 300
gcaggaggac gcttgcacac catgcaggat gacatggggg atgcgctcgg gattggtgtg 360
aagaagcaag gactgttaga ggcaggcttt atagtaacaa gacggtgagg caaactctga 420
tttccgtggg ggaatgtcat ggtcttgctt tactaagttt tgagactggc aggtagtga 480
actcattagg ctgagaacct tgtggaatgc acttgaccca sctgatagag gaagtagcca 540
ggtgggagcc tttcccagtg ggtgtgggac atatctggca agattttgtg gcactcctgg 600
ttacagatac tggggcagca aataaaactg aatcttg 637

<210> 308
<211> 647
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(647)
<223> n = A,T,C or G

<400> 308
 acgattttca ttatcatgta aatcgggtca ctcaaggggc caaccacagc tgggagccac 60
 tgctcagggg aaggttcata tgggactttc tactgcccaa ggttctatac aggatataaa 120
 ggngcctcac agtatagatc tggtagcaaa gaagaagaaa caaacactga tctctttctg 180
 ccacccctct gacccttttg aactcctctg accctttaga acaagcctac ctaatatctg 240
 ctagagaaaa gaccaacaac ggcctcaaag gatctcttac catgaaggtc tcagctaatt 300
 cttggctaag atgtgggttc cacattaggt tctgaatatg gggggaaggg tcaatttgct 360
 cattttgtgt gtggataaag tcaggatgcc cagggggccag agcagggggc tgcttgcttt 420
 gggaacaatg gctgagcata taaccatagg ttatggggaa caaaacaaca tcaaagtcac 480
 tgtatcaatt gccatgaaga cttgagggac ctgaatctac cgattcatct taaggcagca 540
 ggaccagttt gagtggcaac aatgcagcag cagaatcaat ggaaacaaca gaatgattgc 600
 aatgtccttt tttttctcct gcttctgact tgataaaagg ggaccgt 647

<210> 309
 <211> 460
 <212> DNA
 <213> Homo sapien

<400> 309
 actttatagt ttaggctgga cattggaaaa aaaaaaagc cagaacaaca tgtgatagat 60
 aatatgattg gctgcacact tccagactga tgaatgatga acgtgatgga ctattgtatg 120
 gagcacatct tcagcaagag ggggaaatac tcatcatttt tggccagcag ttgtttgatc 180
 accaaacatc atgccagaat actcagcaaa ccttcttagc tcttgagaag tcaaagtcag 240
 ggggaattta ttcttgycaa ttttaattgg actccttatg tgagagcagc ggctaccag 300
 ctggggtggg ggagcgaaac cgtcactagt ggacatgcag tggcagagct cctggtaacc 360
 acctagagga atacacaggc acatgtgtga tgccaagcgt gacacctgta gcactcaaatt 420
 ttgtcttggt tttgtctttc ggtgtgtaag attcttaagt 460

<210> 310
 <211> 539
 <212> DNA
 <213> Homo sapien

<400> 310
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 taggaaagag aaacacagaa ggaagagaca caataaaagt cattatgtat tctgtgagaa 180
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 atgattatgt cattacatgt atggtagtga tggggatgat aggaaggaag aacttatggc 480
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<210> 311
 <211> 526
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)... (526)
 <223> n = A,T,C or G

<400> 311
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 catttacagc atttaaaatg tgttcagcat gaaatatag ctacagggga agctaaataa 180

attaaacatg	gaataaagat	ttgtccttaa	atataatcta	caagaagact	ttgatatttg	240
tttttcacaa	gtgaagcatt	cttataaagt	gtcataacct	ttttggggaa	actatgggaa	300
aaaatgggga	aactctgaag	ggttttaagt	atcttacctg	aagctacaga	ctccataacc	360
tctctttaca	gggagctcct	gcagccctta	cagaaatgag	tggtgagat	tcttgattgc	420
acagcaagag	cttctcatct	aaacccttcc	cctttttagt	atctgtgtat	caagtataaa	480
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<210> 312

<211> 500

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(500)

<223> n = A,T,C or G

<400> 312

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ccatttctct	ttccctcca	cctgccagtt	ttgctgactc	tcaacttgtc	atgagtgtaa	180
gcattaagga	cattatgctt	cttcgattct	gaagacaggc	cctgctcatg	gatgactctg	240
gcttcttagg	aaaatatatt	tcttccaaa	tcagtaggaa	atctaaactt	atccctctct	300
tgcatgctgc	tagcagcttc	agacatttgg	ttaagaacct	atgggaaaaa	aaaaaatcct	360
tgctaattgt	gtttcctttg	ttaaccanga	ttcttatttg	nctggtatag	aatatcagct	420
ctgaacgtgt	ggtaaagatt	tttgtgtttg	aatataggag	aaatcagttt	gctgaaaagt	480
tagtcttaat	tatctattgg					500

<210> 313

<211> 718

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(718)

<223> n = A,T,C or G

<400> 313

ggagatttgt	gtggtttgca	gccgaggag	accaggaaga	tctgcatggt	gggaaggacc	60
tgatgatata	gaggtgagaa	ataagaaagg	ctgctgactt	taccatctga	ggccacacat	120
ctgctgaaat	ggagataatt	aacatcacta	gaaacagcaa	gatgacaata	taatgtctaa	180
gtagtgacat	gtttttgcac	atttcagacc	cttttaata	tccacacaca	caggaagcac	240
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aactggggag	gagataccac	ggggcagagg	tcaggattct	ggccctgctg	cctaactgtg	600
cgttatacca	atcatttcta	tttctaccct	caaacaagct	gtngaatatc	tgacttacgg	660
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<210> 314

<211> 358

<212> DNA

<213> Homo sapien

<400> 314

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caacatgtgt	agatctcttg	tcttattctt	ttgtctataa	tactgtattg	tgtagtccaa	180
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<210> 315

<211> 341

<212> DNA

<213> Homo sapien

<400> 315

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gacccccatt	ctgaagatgt	ctggaacctc	taccagcagg	atgatgatag	ccccaatgac	180
agtcaccagc	tccccgacca	gccggatata	gtccttaggg	gtcatgtagg	cttcctgaag	240
tagcttctgc	tgtaagaggg	tgttgtcccc	ggggctcgtg	cggttattgg	tcctgggctt	300
gagggggcgg	tagatgcagc	acatggtgaa	gcagatgatg	t		341

<210> 316

<211> 151

<212> DNA

<213> Homo sapien

<400> 316

agactgggca	agactcttac	gccccacact	gcaatttggt	cttggtgccg	tatccattta	60
tgtgggcctt	tctcgagttt	ctgattataa	acaccactgg	agcgatgtgt	tgactggact	120
cattcagga	gctctggtg	caatattagt	t			151

<210> 317

<211> 151

<212> DNA

<213> Homo sapien

<400> 317

agaactagtg	gatacctaag	aaatacctga	aacatatatt	ggcattttatc	aatggctcaa	60
atcttcattt	atctctggcc	ttaaccttgg	ctcctgaggg	tgcggccagc	agatcccagg	120
ccagggtct	gttcttgcca	cacctgcttg	a			151

<210> 318

<211> 151

<212> DNA

<213> Homo sapien

<400> 318

actggtggga	ggcgtgttt	agttggetgt	tttcagaggg	gtctttcgga	gggacctcct	60
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tgggggcggt	ttatcaggca	gtgataaaca	t			151

<210> 319

<211> 151

<212> DNA

<213> Homo sapien

<400> 319

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catagatagt	actaggtatt	aatagatatg	taaagaaaga	aatcacacca	ttaataatgg	120

taagattggg tttatgtgat tttagtgggt a 151

<210> 320
 <211> 150
 <212> DNA
 <213> Homo sapien

<400> 320
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 gagcggctgc cctttttttt tttttttttg ggggggaatt tttttttttt aatagttatt 120
 gagtgttcta cagcttacag taaataccat 150

<210> 321
 <211> 151
 <212> DNA
 <213> Homo sapien

<400> 321
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 tagggtggca ttgtaaccag ctatggcata ggtgttaacc aaaggctgag taaacatggg 120
 tgcctctgag aatcaaagt cttcatacac t 151

<210> 322
 <211> 151
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(151)
 <223> n = A,T,C or G

<400> 322
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 tttgggcttg gtcagtttgc cacagggett ggagatgggt acagtcttct ggcattcggc 120
 attgtgcagg gctcgttca nacttcagtt t 151

<210> 323
 <211> 151
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(151)
 <223> n = A,T,C or G

<400> 323
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 nagactcant tactaccag tttgtgggtt twtgggagaa atgtaactgg acagttagct 120
 gttcaatyaa aaagacactt ancccatgtg g 151

<210> 324
 <211> 461
 <212> DNA
 <213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (461)

<223> n = A,T,C or G

<400> 324

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agaagtgggc agctaaagga atccaggttg ttggttggaac tgtaataacc tttgatgaaa	120
agagttacta cgaatcccat cttggttcca gctatatcac tgacagcatg gtagaagact	180
gcgaacctca cttctagact ttcacggtgg gacgaaacgg gttcagaaac tgccaggggc	240
ctcatacagg gatatacaaaa taccctttgt gctaccagg ccctggggaa tcaggtgact	300
cacacaaatg caatagtgtg tcaactgcatt tttacctgaa ccaaagctaa acccggtgtt	360
gccaccatgc accatggcat gccagagttc aacactgttg ctcttgaaaa ttgggtctga	420
aaaaacgcac aagagccct gccctgccct agctgangca c	461

<210> 325

<211> 400

<212> DNA

<213> Homo sapien

<400> 325

acactgtttc catgttatgt ttctacacat tgctacctca gtgtccttg aaacttagct	60
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agtaagagtg gtggcctatt tcagctgctt tgacaaaatg actggctcct gacttaacgt	180
tctataaatg aatgtgctga agcaaatggt ccatgggtggc ggcaagaag agaaagatgt	240
gtttgtttt ggactctctg tgggtccctc caatgctgtg ggtttccaac caggggaagg	300
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<210> 326

<211> 1215

<212> DNA

<213> Homo sapien

<400> 326

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gaactcctac accatcgggc tgggcctgca cagtcttgag gccgaccaag agccagggag	180
ccagatggtg gaggccagcc tctccgtacg gcaccagag tacaacagac ccttgctcgc	240
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<210> 327

<211> 220

<212> PRT

<213> Homo sapien

<400> 327

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Glu Asp Cys Ser Pro His Ser Gln Pro Trp Gln Ala Ala Leu Val Met
 1          5          10          15
Glu Asn Glu Leu Phe Cys Ser Gly Val Leu Val His Pro Gln Trp Val
          20          25          30
Leu Ser Ala Ala His Cys Phe Gln Asn Ser Tyr Thr Ile Gly Leu Gly
          35          40          45
Leu His Ser Leu Glu Ala Asp Gln Glu Pro Gly Ser Gln Met Val Glu
          50          55          60
Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg Pro Leu Leu Ala
65          70          75          80
Asn Asp Leu Met Leu Ile Lys Leu Asp Glu Ser Val Ser Glu Ser Asp
          85          90          95
Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln Cys Pro Thr Ala Gly Asn
          100          105          110
Ser Cys Leu Val Ser Gly Trp Gly Leu Leu Ala Asn Gly Arg Met Pro
          115          120          125
Thr Val Leu Gln Cys Val Asn Val Ser Val Val Ser Glu Glu Val Cys
          130          135          140
Ser Lys Leu Tyr Asp Pro Leu Tyr His Pro Ser Met Phe Cys Ala Gly
145          150          155          160
Gly Gly Gln Asp Gln Lys Asp Ser Cys Asn Gly Asp Ser Gly Gly Pro
          165          170          175
Leu Ile Cys Asn Gly Tyr Leu Gln Gly Leu Val Ser Phe Gly Lys Ala
          180          185          190
Pro Cys Gly Gln Val Gly Val Pro Gly Val Tyr Thr Asn Leu Cys Lys
          195          200          205
Phe Thr Glu Trp Ile Glu Lys Thr Val Gln Ala Ser
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<210> 328

<211> 234

<212> DNA

<213> Homo sapien

<400> 328

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atccgcagtg ggtgctgtca gccacacact gtttcagaa ctctacacc atcgggctgg      180
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<210> 329

<211> 77

<212> PRT

<213> Homo sapien

<400> 329

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Leu Val Ser Gly Ser Cys Ser Gln Ile Ile Asn Gly Glu Asp Cys Ser
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Pro His Ser Gln Pro Trp Gln Ala Ala Leu Val Met Glu Asn Glu Leu
          20          25          30
Phe Cys Ser Gly Val Leu Val His Pro Gln Trp Val Leu Ser Ala Thr
          35          40          45
His Cys Phe Gln Asn Ser Tyr Thr Ile Gly Leu Gly Leu His Ser Leu
          50          55          60

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Glu Ala Asp Gln Glu Pro Gly Ser Gln Met Val Glu Ala
65 70 75

<210> 330
<211> 70
<212> DNA
<213> Homo sapien

<400> 330
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gctgcagcca 70

<210> 331
<211> 22
<212> PRT
<213> Homo sapien

<400> 331
Gln His Asn Gly Pro Ile Pro Ser Leu Thr Pro Pro Ser Gly Ser Leu
1 5 10 15
Val Ser Gly Ser Cys Ser
20

<210> 332
<211> 2507
<212> DNA
<213> Homo sapien

<400> 332
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<210> 333

<211> 3030

<212> DNA

<213> Homo sapien

<400> 333

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<211> 2417

<212> DNA

<213> Homo sapien

<400> 334

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 <213> Homo sapien

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 <212> PRT
 <213> Homo sapien

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 35 40 45
 Val Ile Glu Leu Glu Arg Lys Phe Ser His Gln Lys Tyr Leu Ser Ala
 50 55 60
 Pro Glu Arg Ala His Leu Ala Lys Asn Leu Lys Leu Thr Glu Thr Gln
 65 70 75 80
 Val Lys Ile Trp Phe Gln Asn Arg Arg Tyr Lys Thr Lys Arg Lys Gln
 85 90 95
 Leu Ser Ser Glu Leu Gly Asp Leu Glu Lys His Ser Ser Leu Pro Ala
 100 105 110
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 Ser Tyr Pro Tyr Tyr Pro Tyr Leu Tyr Cys Val Gly Ser Trp Ser Pro
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 Ala Phe Trp
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 <212> PRT
 <213> Homo sapien

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<211> 483
<212> DNA
<213> Homo sapien
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<211> 344
<212> DNA
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<211> 592

<212> DNA

<213> Homo sapien

<400> 342

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<210> 343

<211> 382

<212> DNA

<213> Homo sapien

<400> 343

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<210> 344

<211> 536

<212> DNA

<213> Homo sapien

<400> 344

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<210> 345

<211> 251

<212> DNA

<213> Homo sapien

<400> 345

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<210> 346

<211> 282

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

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<223> n = A,T,C or G

<400> 346

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<210> 347

<211> 201

<212> DNA

<213> Homo sapien

<220>

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<222> (1)...(201)

<223> n = A,T,C or G

<400> 347

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<210> 348

<211> 251

<212> DNA

<213> Homo sapien

<400> 348

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<210> 349

<211> 251

<212> DNA

<213> Homo sapien

<400> 349

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cagaaggggc tgaactctac gtgttaccag agaacataat gcaattcatg cattccactt	180
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<210> 350

<211> 908

<212> DNA

<213> Homo sapien

<400> 350

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gttcaagtgc aacaatgact atgtgcctgt gtgtggctcc aatggggaga gctaccagaa	300
tgagtgttac ctgacagagg ctgcatgcaa acagcagagt gagatacttg tgggtgcaga	360
aggatcatgt gccacagtc atgaaggctc tggagaaact agtcaaaagg agacatccac	420
ctgtgatatt tgcagtttg gtgcagaatg tgacgaagat gccgaggatg tctggtgtgt	480
gtgtaatat gactgttctc aaaccaactt caatccctc tgcgcttctg atgggaaatc	540
ttatgataat gcatgccaaa tcaaagaagc atcgtgtcag aaacaggaga aaattgaagt	600
catgtctttg ggtcgtatgc aagataacac aactacaact actaagtctg aagatgggca	660
ttatgcaaga acagattatg cagagaatgc taacaaatta gaagaaagtg ccagagaaca	720
ccacatacct tgtccggaac attacaatgg ctctctcatg catgggaagt gtgagcatte	780
tatcaatatg caggagccat cttgcagggt tgatgctggg tatactggac aacactgtga	840
aaaaaaggac tacagtgttc tatacgttgt tcccggctct gtaacgatttc agtatgtctt	900
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<210> 351

<211> 472

<212> DNA

<213> Homo sapien

<400> 351

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cattaacttg attttaaaat cagwtttgyg agtcattttac cacaagctaa atgtgtacac	180
tatgataaaa acaaccattg tattcctgtt tttctaaaca gtccataattt ctaacactgt	240
atatatcctt cgacatcaat gaactttgtt ttcttttact ccagtaataa agtaggcaca	300
gatctgtcca caacaaactt gccctctcat gccttgctc tcacatgct ctgctccagg	360
tcagccccc tttggcctgt ttgttttgtc aaaaacctaa tctgcttctt gcttttcttg	420
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<210> 352

<211> 251

<212> DNA

<213> Homo sapien

<400> 352

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caggctcgt tccgtcctta cgatgaagac cagcatgcag tttccaaaca ttgccactac	180
atacatggaa aggaggggga agccaacca gaaatgggct ttctctaate ctgggatacc	240
aataagcaca a	251

<210> 353
 <211> 436
 <212> DNA
 <213> Homo sapien

<400> 353
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 gtatccaaaa gcaaaacagc agatatacaa aattaaagag acagaagata gacattaaca 180
 gataaggcaa cttatacatt gacaatccaa atccaatata tttaaacatt tgggaaatga 240
 gggggacaaa tggaagccar atcaaatttg tgtaaaacta ttcagtatgt ttccttgcct 300
 tcatgtctga raaggctctc ccttcaatgg ggatgacaaa ctccaaatgc cacacaaatg 360
 ttaacagaat actagattca cactggaacg ggggtaaaaga agaaattatt ttctataaaa 420
 gggctcctaa tgtagt 436

<210> 354
 <211> 854
 <212> DNA
 <213> Homo sapien

<400> 354
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 atcagggacc accctttggg ttgatatttt gcttaatctg catcttttga gtaagatcat 180
 ctggcagtag aagctgttct ccagggtacat ttctctagct catgtacaaa aacatcctga 240
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 ttaattgcac acctacaggc actgggctca tgctttcaag tattttgtcc tcactttagg 360
 gtgagtgaat gatccccatt ataggagcac ttgggagaga tcatataaaa gctgactcct 420
 gagtacatgc agtaatgggg tagatgtgtg tgggtgtgtc tcattcctgc aagggtgctt 480
 gttaggaggt gtttccagga ggaacaagtc tgaaaccaat catgaaataa atggtaggtg 540
 tgaactggaa aactaattca aaagagagat cgtgatatac gtgtgggtga tacaccttgg 600
 caatatggaa ggctctaatt tgcccatatt tgaaataata attcagcttt ttgtaataca 660
 aaataacaaa ggattgagaa tcatggtgtc taatgtataa aagaccaggg aaacataaat 720
 atatcaactg cataaatgta aaatgcatgt gaccacaaga gggcccaaaag tggcagacaa 780
 cattgtaccc attttccctt ccaaaatgtg agcggcgggc ctgctgcttt caaggctgtc 840
 acacgggatg tcag 854

<210> 355
 <211> 676
 <212> DNA
 <213> Homo sapien

<400> 355
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 atccacaagt catacctgga tgtcagcgaa gagggcacgg aggcagcagc agccactggg 180
 gacagcatcg ctgtaaaaag cctaccaatg agagctcagt tcaaggcgaa ccacccttc 240
 ctgttcttta taaggcacac tcataccaac acgatcctat tctgtggcaa gcttgcctct 300
 ccctaatacag atgggggtga gtaaggctca gagttgcaga tgagggtcag agacaatcct 360
 gtgactttcc cagggccaaa aagctgttca cacctcacgc acctctgtgc ctgactttgc 420
 tcatctgcaa aataggtcta ggatttcttc caaccatttc atgagttgtg aagctaaggc 480
 tttgttaatc atggaaaaag gtatagcttat gcagaaaaggc tttctggctt tcttatctgt 540
 ggtgtctcat ttgagtgtg tccagtgaac tgatcaagtc aatgagttaa attttaaggg 600
 attagatttt cttgacttgt atgtatctgt gagatcttga ataagtgacc tgacatctct 660
 gcttaaagaa aaccag 676

<210> 356

<211> 574
 <212> DNA
 <213> Homo sapien

<400> 356

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caagcttccc	atttgtagat	ctcagtgcct	atgagtatct	gacacctgtt	cctctcttca	180
gtctcttagg	gaggcttaaa	tctgtctcag	gtgtgctaag	agtgccagcc	caaggkggtc	240
aaaagtccac	aaaactgcag	tctttgctgg	gatagtaagc	caagcagtgc	ctggacagca	300
gagttctttt	cttgggcaac	agataaccag	acaggactct	aatcgtgctc	ttattcaaca	360
ttcttctgtc	tctgcctaga	ctggaataaa	aagccaatct	ctctcgtggc	acaggggaagg	420
agatacaagc	tcgtttacat	gtgatagatc	taacaaaggc	atctaccgaa	gtctggtctg	480
gatagacggc	acagggagct	cttaggtcag	cgctgctggg	tggaggacat	tcttgagtcc	540
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<210> 357
 <211> 393
 <212> DNA
 <213> Homo sapien

<400> 357

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taatatggkg	kcttgttcac	tatacttaaa	aatgcaccac	tcataaatat	ttaattcagc	120
aagccacaac	caaracttga	ttttatcaac	aaaaaccctt	aaatataaac	ggsaaaaaag	180
atagatataa	ttattccagt	ttttttaaaa	cttaaaarat	attccattgc	cgaattaara	240
araarataag	tgttatatgg	aaagaagggc	attcaagcac	actaaaraaa	cctgaggkaa	300
gcataatctg	tacaaaatta	aactgtcctt	tttggcattt	taacaaattt	gcaacgktct	360
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<210> 358
 <211> 630
 <212> DNA
 <213> Homo sapien

<400> 358

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gcatagagta	gggaagctaa	tccagcacag	ggaggtcaca	gagacatccc	taaggaagtg	180
gagttaaac	tgagagaagc	aagtgtctaa	actgaaggat	gtgttgaaga	agaagggaga	240
gtagaacaat	ttgggcagag	ggaaccttat	agaccctaag	gtgggaagg	tcaaagaact	300
gaaagagagc	tagaacagct	ggagccgttc	tccgggtgta	agaggagtca	aagagataag	360
attaaagatg	tgaagattaa	gatcttggtg	gcattcaggg	attggcactt	ctacaagaaa	420
tactgaagg	gagtaatgtg	acattacttt	tacttcagg	atggccattc	taactccagg	480
gggtagactg	gactaggtaa	gactggaggg	aggtagacct	cttctaaggc	ctgcgatagt	540
gaaagacaaa	aataagtggg	gaaattcagg	ggatagtga	aatcagtagg	acttaatgag	600
caagccagag	gttcctccac	aacaaccagt				630

<210> 359
 <211> 620
 <212> DNA
 <213> Homo sapien

<400> 359

acagcattcc	aaaatataca	tctagagact	aarrgtaaat	gctctatagt	gaagaagtaa	60
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ctcaccagaa	gaataaagtg	ctctgccagt	tattaaagga	ttactgctgg	tgaattaaat	180
atggcattcc	ccaagggaaa	tagagagatt	cttctggatt	atgttcaata	tttatttcac	240

aggattaact	gttttaggaa	cagatataaa	gcttcgccac	ggaagagatg	gacaaagcac	300
aaagacaaca	tgatacctta	ggaagcaaca	ctaccctttc	aggcataaaa	tttgaggaaa	360
tgcaacatta	tgcttcatga	ataatatgta	gaaagaagggt	ctgatgaaaa	tgacatcctt	420
aatgtaagat	aactttataa	gaattctggg	tcaaataaaa	ttctttgaag	aaaacatcca	480
aatgtcattg	acttatcaaa	tactatcttg	gcatataacc	tatgaaggca	aaactaaaca	540
aacaaaaagc	tcacaccaa	caaaaccatc	aacttatttt	gtattctata	acatacgaga	600
ctgtaaagat	gtgacagtgt					620

<210> 360

<211> 431

<212> DNA

<213> Homo sapien

<400> 360

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tactcatcat	ttttggccag	cagttgtttg	atcaccaaac	atcatgccag	aatactcagc	180
aaaccttctt	agctcttgag	aagtcaaagt	ccgggggaat	ttattcctgg	caattttaat	240
tggactcctt	atgtgagagc	agcggctacc	cagctggggg	ggtggagcga	acccgtcact	300
agtgagacatg	cagtggcaga	gctcctggta	accacctaga	ggaatacaca	ggcacatgtg	360
tgatgccaaag	cgtgacacct	gtagcactca	aatttgtctt	gtttttgtct	ttcgggtgtgt	420
agattcttag	t					431

<210> 361

<211> 351

<212> DNA

<213> Homo sapien

<400> 361

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caatcctgga	ttcaatgtct	gaaacctcgc	tctctgctcg	ctggacttct	gaggccgtca	300
ctgccactct	gtcctccagc	tctgacagct	cctcatctgt	ggtcctgttg	t	351

<210> 362

<211> 463

<212> DNA

<213> Homo sapien

<400> 362

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ccccggtcac	agaaatgacc	aggttgggtg	ttttcagggt	ccagtgtctg	gtcagcagct	180
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agttccattt	ctcactttgg	ttgatctggg	tgccttccat	gtgctggctc	tgggcatagc	360
cacacttgca	cacatttctc	ctgataagca	cgatggtgtg	gacaggaagg	aaggatttca	420
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<210> 363

<211> 653

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (653)

<223> n = A,T,C or G

<400> 363

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ccaacagcaa	ccccccggaa	gtatgagttc	ctctrgggcc	tccgttccta	ccatgagasc	300
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ntgggcccctg	gagctgggat	gacattgagt	ttgagctgct	gacctgggat	gaggaaggag	540
attttggaga	tccttggtcc	agaattccat	ttacctctctg	ggccagatac	caccagaatg	600
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<210> 364

<211> 401

<212> DNA

<213> Homo sapien

<400> 364

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aaaacaaggt	ggatagatct	agaattgtaa	cattttaaga	aaaccatagc	atttgacaga	180
tgagaaagct	caattataga	tgcaaagtta	taactaaact	actatagtag	taaagaaata	240
catttcacac	ccttcatata	aattcactat	cttggcttga	ggcactccat	aaaatgtatc	300
acgtgcatag	taaatcttta	tatttgctat	ggcgttgac	tagaggactt	ggactgcaac	360
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<210> 365

<211> 356

<212> DNA

<213> Homo sapien

<400> 365

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gactgtcacg	atgtgtatag	tacagtttga	caagcctggg	tccatacaga	ccgctggaga	300
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<210> 366

<211> 1851

<212> DNA

<213> Homo sapien

<400> 366

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tcacttccct	taagcctttg	tgactcttcc	tctgatgtca	gctttaagtc	ttgttctgga	180
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tgattaaaaa	tttcaccact	tgctgttttt	gctcatgtat	accaagtagc	agtgggtgtg	480
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atttatcttc	attgtagaca	gcatagtgta	gagtgggtatt	tccataactca	tctggaatat	600
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cctttgtcag	agctgtcctc	tttttgttgt	caaggacatt	aagttgacat	cgtctgtcca	720
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<210> 367

<211> 668

<212> DNA

<213> Homo sapien

<400> 367

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accrtataag	agcagtgcct	tggccattaa	tttatcttct	atrttagaca	gcrtagtgya	180
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aogcacattc	atcttcctgg	cattgtacgg	cctgtcagta	ttagacccaa	aaacaaatta	300
catatcttag	gaattcaaaa	taacattcca	cagcttccac	caactagtta	tattttaaagg	360
agaaaactca	tttttatgcc	atgtattgaa	atcaaaccce	cctcatgctg	atatagttgg	420
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gcagtcctat	gagagtgaga	agacttttta	ggaaattgta	gtgcactagc	tacagccata	600
gcaatgatcc	atgtaactgc	aaacactgaa	tagcctgcta	ttactctgcc	ttcaaaaaaa	660
aaaaaaaa						668

<210> 368

<211> 1512

<212> DNA

<213> Homo sapien

<400> 368

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aacaagaagg	acaagcaaaa	gaggactgct	ctacatctgg	cctctgcca	tgggaattca	780
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<210> 369

<211> 1853

<212> DNA

<213> Homo sapien

<400> 369

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<210> 370

<211> 2184

<212> DNA

<213> Homo sapien

<400> 370

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<210> 371

<211> 1855

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(1855)

<223> n = A,T,C or G

<400> 371

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<210> 372

<211> 1059

<212> DNA

<213> Homo sapien

<400> 372

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<210> 373

<211> 1155

<212> DNA

<213> Homo sapien

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<210> 374

<211> 2000

<212> DNA

<213> Homo sapien

<400> 374

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<210> 375
 <211> 2040
 <212> DNA
 <213> Homo sapien

<400> 375
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 gccagagagt atgctgttcc tagtcatcat catgtaattt gccagtact ttctgactac 1080
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 ctgacatcag aggaagagtc acaaagggtc aaaggcagtg aaaaatagcca gccagagaaa 1200
 atgtctcaag aaccagaaat aaataaggat ggtgatagag aggttgaaga agaaatgaag 1260
 aagcatgaaa gtaataatgt gggattacta gaaaacctga ctaatggtgt cactgctggc 1320
 aatggtgata atggattaat tcctcaaagg aagagcagaa cacctgaaaa tcagcaattt 1380
 cctgacaacg aaagtgaaga gtatcacaga atttgcgaat tagtttctga ctacaaagaa 1440
 aaacagatgc caaaatactc ttctgaaaac agcaaccag aacaagactt aaagctgaca 1500
 tcagaggaag agtcacaaag gcttgagggc agtgaaaatg gccagccaga gaaaagatct 1560
 caagaaccag aaataaataa ggatggtgat agagagctag aaaattttat ggctatcgaa 1620
 gaaatgaaga agcacggaag tactcatgtc ggattcccag aaaacctgac taatggtgcc 1680
 actgctggca atggtgatga tggattaatt cctccaagga agagcagaac acctgaaagc 1740
 cagcaatttc ctgacactga gaatgaagag tatcacagt acgaacaaaa tgatactcag 1800
 aagcaatttt gtgaagaaca gaacactgga atattacacg atgagattct gattcatgaa 1860
 gaaaagcaga tagaagtggg tgaaaaaatg aattctgagc tttctcttag ttgtaagaaa 1920
 gaaaaagaca tcttgcatga aaatagtacg ttgcgggaag aaattgccat gctaagactg 1980
 gagctagaca caatgaaca tcagagccag ctaaaaaaa aaaaaaaaaa aaaaaaaaaa 2040

<210> 376
 <211> 329
 <212> PRT
 <213> Homo sapien

<400> 376
 Met Asp Ile Val Val Ser Gly Ser His Pro Leu Trp Val Asp Ser Phe
 1 5 10 15
 Leu His Leu Ala Gly Ser Asp Leu Leu Ser Arg Ser Leu Met Ala Glu
 20 25 30
 Glu Tyr Thr Ile Val His Ala Ser Phe Ile Ser Cys Ile Ser Ser Ser
 35 40 45
 Leu Asp Gly Gln Gly Glu Arg Gln Glu Gln Arg Gly His Phe Trp Arg
 50 55 60


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Pro Gln Arg Leu Leu Cys Glu Asp Ala Trp Glu Gln Glu Val Gln Val
65          70          75          80
Val Leu Pro Leu Leu Pro Leu Leu Gln Gly Ser Gly Lys Ser Asn Val
      85          90          95
Val Ala Trp Gly Asp Tyr Asp Asp Ser Ala Phe Met Asp Pro Arg Tyr
      100        105        110
His Val His Gly Glu Asp Leu Asp Lys Leu His Arg Ala Ala Trp Trp
      115        120        125
Gly Lys Val Pro Arg Lys Asp Leu Ile Val Met Leu Arg Asp Thr Asp
      130        135        140
Val Asn Lys Arg Asp Lys Gln Lys Arg Thr Ala Leu His Leu Ala Ser
145          150          155          160
Ala Asn Gly Asn Ser Glu Val Val Lys Leu Val Leu Asp Arg Arg Cys
      165        170        175
Gln Leu Asn Val Leu Asp Asn Lys Lys Arg Thr Ala Leu Thr Lys Ala
      180        185        190
Val Gln Cys Gln Glu Asp Glu Cys Ala Leu Met Leu Leu Glu His Gly
      195        200        205
Thr Asp Pro Asn Ile Pro Asp Glu Tyr Gly Asn Thr Thr Leu His Tyr
      210        215        220
Ala Val Tyr Asn Glu Asp Lys Leu Met Ala Lys Ala Leu Leu Leu Tyr
225          230          235          240
Gly Ala Asp Ile Glu Ser Lys Asn Lys His Gly Leu Thr Pro Leu Leu
      245        250        255
Leu Gly Ile His Glu Gln Lys Gln Gln Val Val Lys Phe Leu Ile Lys
      260        265        270
Lys Lys Ala Asn Leu Asn Ala Leu Asp Arg Tyr Gly Arg Thr Ala Leu
      275        280        285
Ile Leu Ala Val Cys Cys Gly Ser Ala Ser Ile Val Ser Pro Leu Leu
      290        295        300
Glu Gln Asn Val Asp Val Ser Ser Gln Asp Leu Glu Arg Arg Pro Glu
305          310          315          320
Ser Met Leu Phe Leu Val Ile Ile Met
      325

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<210> 377
<211> 148
<212> PRT
<213> Homo sapien

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<220>
<221> VARIANT
<222> (1)...(148)
<223> Xaa = Any Amino Acid

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<400> 377
Met Thr Xaa Pro Ser Trp Ser Pro Gly Thr Thr Ser Val Glu Lys Ile
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Trp Thr Ser Ser Thr Glu Leu Pro Trp Trp Gly Lys Val Pro Arg Lys
      20          25          30
Asp Leu Ile Val Met Leu Arg Asp Thr Asp Val Asn Lys Xaa Asp Lys
      35          40          45
Gln Lys Arg Thr Ala Leu His Leu Ala Ser Ala Asn Gly Asn Ser Glu
      50          55          60
Val Val Lys Leu Xaa Leu Asp Arg Arg Cys Gln Leu Asn Val Leu Asp
65          70          75          80
Asn Lys Lys Arg Thr Ala Leu Xaa Lys Ala Val Gln Cys Gln Glu Asp
      85          90          95

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Glu Cys Ala Leu Met Leu Leu Glu His Gly Thr Asp Pro Asn Ile Pro
 100 105 110
 Asp Glu Tyr Gly Asn Thr Thr Leu His Tyr Ala Xaa Tyr Asn Glu Asp
 115 120 125
 Lys Leu Met Ala Lys Ala Leu Leu Leu Tyr Gly Ala Asp Ile Glu Ser
 130 135 140
 Lys Asn Lys Val
 145

<210> 378
 <211> 1719
 <212> PRT
 <213> Homo sapien

<400> 378
 Met Val Val Glu Val Asp Ser Met Pro Ala Ala Ser Ser Val Lys Lys
 1 5 10 15
 Pro Phe Gly Leu Arg Ser Lys Met Gly Lys Trp Cys Cys Arg Cys Phe
 20 25 30
 Pro Cys Cys Arg Glu Ser Gly Lys Ser Asn Val Gly Thr Ser Gly Asp
 35 40 45
 His Asp Asp Ser Ala Met Lys Thr Leu Arg Ser Lys Met Gly Lys Trp
 50 55 60
 Cys Arg His Cys Phe Pro Cys Cys Arg Gly Ser Gly Lys Ser Asn Val
 65 70 75 80
 Gly Ala Ser Gly Asp His Asp Asp Ser Ala Met Lys Thr Leu Arg Asn
 85 90 95
 Lys Met Gly Lys Trp Cys Cys His Cys Phe Pro Cys Cys Arg Gly Ser
 100 105 110
 Gly Lys Ser Lys Val Gly Ala Trp Gly Asp Tyr Asp Asp Ser Ala Phe
 115 120 125
 Met Glu Pro Arg Tyr His Val Arg Gly Glu Asp Leu Asp Lys Leu His
 130 135 140
 Arg Ala Ala Trp Trp Gly Lys Val Pro Arg Lys Asp Leu Ile Val Met
 145 150 155 160
 Leu Arg Asp Thr Asp Val Asn Lys Lys Asp Lys Gln Lys Arg Thr Ala
 165 170 175
 Leu His Leu Ala Ser Ala Asn Gly Asn Ser Glu Val Val Lys Leu Leu
 180 185 190
 Leu Asp Arg Arg Cys Gln Leu Asn Val Leu Asp Asn Lys Lys Arg Thr
 195 200 205
 Ala Leu Ile Lys Ala Val Gln Cys Gln Glu Asp Glu Cys Ala Leu Met
 210 215 220
 Leu Leu Glu His Gly Thr Asp Pro Asn Ile Pro Asp Glu Tyr Gly Asn
 225 230 235 240
 Thr Thr Leu His Tyr Ala Ile Tyr Asn Glu Asp Lys Leu Met Ala Lys
 245 250 255
 Ala Leu Leu Leu Tyr Gly Ala Asp Ile Glu Ser Lys Asn Lys His Gly
 260 265 270
 Leu Thr Pro Leu Leu Leu Gly Val His Glu Gln Lys Gln Gln Val Val
 275 280 285
 Lys Phe Leu Ile Lys Lys Lys Ala Asn Leu Asn Ala Leu Asp Arg Tyr
 290 295 300
 Gly Arg Thr Ala Leu Ile Leu Ala Val Cys Cys Gly Ser Ala Ser Ile
 305 310 315 320
 Val Ser Leu Leu Leu Glu Gln Asn Ile Asp Val Ser Ser Gln Asp Leu
 325 330 335
 Ser Gly Gln Thr Ala Arg Glu Tyr Ala Val Ser Ser His His His Val

Ile	Cys	Gln	340	Leu	Leu	Ser	Asp	Tyr	345	Lys	Glu	Lys	Gln	Met	350	Leu	Lys	Ile
		355						360						365				
Ser	Ser	Glu	Asn	Ser	Asn	Pro	Glu	Asn	Val	Ser	Arg	Thr	Arg	Asn	Lys			
		370				375					380							
Pro	Arg	Thr	His	Met	Val	Val	Glu	Val	Asp	Ser	Met	Pro	Ala	Ala	Ser			
385				390					395						400			
Ser	Val	Lys	Lys	Pro	Phe	Gly	Leu	Arg	Ser	Lys	Met	Gly	Lys	Trp	Cys			
			405					410						415				
Cys	Arg	Cys	Phe	Pro	Cys	Cys	Arg	Glu	Ser	Gly	Lys	Ser	Asn	Val	Gly			
		420						425					430					
Thr	Ser	Gly	Asp	His	Asp	Asp	Ser	Ala	Met	Lys	Thr	Leu	Arg	Ser	Lys			
		435					440					445						
Met	Gly	Lys	Trp	Cys	Arg	His	Cys	Phe	Pro	Cys	Cys	Arg	Gly	Ser	Gly			
		450				455					460							
Lys	Ser	Asn	Val	Gly	Ala	Ser	Gly	Asp	His	Asp	Asp	Ser	Ala	Met	Lys			
465				470						475					480			
Thr	Leu	Arg	Asn	Lys	Met	Gly	Lys	Trp	Cys	Cys	His	Cys	Phe	Pro	Cys			
			485					490						495				
Cys	Arg	Gly	Ser	Gly	Lys	Ser	Lys	Val	Gly	Ala	Trp	Gly	Asp	Tyr	Asp			
		500						505					510					
Asp	Ser	Ala	Phe	Met	Glu	Pro	Arg	Tyr	His	Val	Arg	Gly	Glu	Asp	Leu			
		515					520					525						
Asp	Lys	Leu	His	Arg	Ala	Ala	Trp	Trp	Gly	Lys	Val	Pro	Arg	Lys	Asp			
		530				535					540							
Leu	Ile	Val	Met	Leu	Arg	Asp	Thr	Asp	Val	Asn	Lys	Lys	Asp	Lys	Gln			
545				550						555					560			
Lys	Arg	Thr	Ala	Leu	His	Leu	Ala	Ser	Ala	Asn	Gly	Asn	Ser	Glu	Val			
			565					570						575				
Val	Lys	Leu	Leu	Leu	Asp	Arg	Arg	Cys	Gln	Leu	Asn	Val	Leu	Asp	Asn			
		580						585					590					
Lys	Lys	Arg	Thr	Ala	Leu	Ile	Lys	Ala	Val	Gln	Cys	Gln	Glu	Asp	Glu			
		595					600					605						
Cys	Ala	Leu	Met	Leu	Leu	Glu	His	Gly	Thr	Asp	Pro	Asn	Ile	Pro	Asp			
		610				615				620								
Glu	Tyr	Gly	Asn	Thr	Thr	Leu	His	Tyr	Ala	Ile	Tyr	Asn	Glu	Asp	Lys			
625				630						635					640			
Leu	Met	Ala	Lys	Ala	Leu	Leu	Leu	Tyr	Gly	Ala	Asp	Ile	Glu	Ser	Lys			
			645					650					655					
Asn	Lys	His	Gly	Leu	Thr	Pro	Leu	Leu	Leu	Gly	Val	His	Glu	Gln	Lys			
		660					665						670					
Gln	Gln	Val	Val	Lys	Phe	Leu	Ile	Lys	Lys	Lys	Ala	Asn	Leu	Asn	Ala			
		675					680					685						
Leu	Asp	Arg	Tyr	Gly	Arg	Thr	Ala	Leu	Ile	Leu	Ala	Val	Cys	Cys	Gly			
		690				695					700							
Ser	Ala	Ser	Ile	Val	Ser	Leu	Leu	Leu	Glu	Gln	Asn	Ile	Asp	Val	Ser			
705				710						715					720			
Ser	Gln	Asp	Leu	Ser	Gly	Gln	Thr	Ala	Arg	Glu	Tyr	Ala	Val	Ser	Ser			
			725					730						735				
His	His	His	Val	Ile	Cys	Gln	Leu	Leu	Ser	Asp	Tyr	Lys	Glu	Lys	Gln			
			740					745					750					
Met	Leu	Lys	Ile	Ser	Ser	Glu	Asn	Ser	Asn	Pro	Glu	Gln	Asp	Leu	Lys			
		755					760					765						
Leu	Thr	Ser	Glu	Glu	Glu	Ser	Gln	Arg	Phe	Lys	Gly	Ser	Glu	Asn	Ser			
		770				775					780							
Gln	Pro	Glu	Lys	Met	Ser	Gln	Glu	Pro	Glu	Ile	Asn	Lys	Asp	Gly	Asp			
785				790						795					800			
Arg	Glu	Val	Glu	Glu	Glu	Met	Lys	Lys	His	Glu	Ser	Asn	Asn	Val	Gly			

Leu	Leu	Glu	Asn	Leu	Thr	Asn	Gly	Val	Thr	Ala	Gly	Asn	Gly	Asp	Asn
			820					825					830		
Gly	Leu	Ile	Pro	Gln	Arg	Lys	Ser	Arg	Thr	Pro	Glu	Asn	Gln	Gln	Phe
		835					840					845			
Pro	Asp	Asn	Glu	Ser	Glu	Glu	Tyr	His	Arg	Ile	Cys	Glu	Leu	Val	Ser
		850					855				860				
Asp	Tyr	Lys	Glu	Lys	Gln	Met	Pro	Lys	Tyr	Ser	Ser	Glu	Asn	Ser	Asn
865					870					875					880
Pro	Glu	Gln	Asp	Leu	Lys	Leu	Thr	Ser	Glu	Glu	Glu	Ser	Gln	Arg	Leu
			885						890					895	
Glu	Gly	Ser	Glu	Asn	Gly	Gln	Pro	Glu	Leu	Glu	Asn	Phe	Met	Ala	Ile
			900					905					910		
Glu	Glu	Met	Lys	Lys	His	Gly	Ser	Thr	His	Val	Gly	Phe	Pro	Glu	Asn
		915					920					925			
Leu	Thr	Asn	Gly	Ala	Thr	Ala	Gly	Asn	Gly	Asp	Asp	Gly	Leu	Ile	Pro
		930				935					940				
Pro	Arg	Lys	Ser	Arg	Thr	Pro	Glu	Ser	Gln	Gln	Phe	Pro	Asp	Thr	Glu
945					950					955					960
Asn	Glu	Glu	Tyr	His	Ser	Asp	Glu	Gln	Asn	Asp	Thr	Gln	Lys	Gln	Phe
			965						970					975	
Cys	Glu	Glu	Gln	Asn	Thr	Gly	Ile	Leu	His	Asp	Glu	Ile	Leu	Ile	His
			980					985					990		
Glu	Glu	Lys	Gln	Ile	Glu	Val	Val	Glu	Lys	Met	Asn	Ser	Glu	Leu	Ser
		995					1000					1005			
Leu	Ser	Cys	Lys	Lys	Glu	Lys	Asp	Ile	Leu	His	Glu	Asn	Ser	Thr	Leu
		1010				1015						1020			
Arg	Glu	Glu	Ile	Ala	Met	Leu	Arg	Leu	Glu	Leu	Asp	Thr	Met	Lys	His
1025					1030					1035					1040
Gln	Ser	Gln	Leu	Pro	Arg	Thr	His	Met	Val	Val	Glu	Val	Asp	Ser	Met
			1045						1050					1055	
Pro	Ala	Ala	Ser	Ser	Val	Lys	Lys	Pro	Phe	Gly	Leu	Arg	Ser	Lys	Met
			1060					1065					1070		
Gly	Lys	Trp	Cys	Cys	Arg	Cys	Phe	Pro	Cys	Cys	Arg	Glu	Ser	Gly	Lys
		1075					1080					1085			
Ser	Asn	Val	Gly	Thr	Ser	Gly	Asp	His	Asp	Asp	Ser	Ala	Met	Lys	Thr
		1090				1095						1100			
Leu	Arg	Ser	Lys	Met	Gly	Lys	Trp	Cys	Arg	His	Cys	Phe	Pro	Cys	Cys
1105					1110					1115					1120
Arg	Gly	Ser	Gly	Lys	Ser	Asn	Val	Gly	Ala	Ser	Gly	Asp	His	Asp	Asp
			1125						1130					1135	
Ser	Ala	Met	Lys	Thr	Leu	Arg	Asn	Lys	Met	Gly	Lys	Trp	Cys	Cys	His
		1140						1145					1150		
Cys	Phe	Pro													

1265	1270	1275	1280
Asn Ile Pro Asp Glu Tyr Gly Asn Thr Thr Leu His Tyr Ala Ile Tyr			
1285	1290	1295	
Asn Glu Asp Lys Leu Met Ala Lys Ala Leu Leu Leu Tyr Gly Ala Asp			
1300	1305	1310	
Ile Glu Ser Lys Asn Lys His Gly Leu Thr Pro Leu Leu Leu Gly Val			
1315	1320	1325	
His Glu Gln Lys Gln Gln Val Val Lys Phe Leu Ile Lys Lys Lys Ala			
1330	1335	1340	
Asn Leu Asn Ala Leu Asp Arg Tyr Gly Arg Thr Ala Leu Ile Leu Ala			
1345	1350	1355	1360
Val Cys Cys Gly Ser Ala Ser Ile Val Ser Leu Leu Leu Glu Gln Asn			
1365	1370	1375	
Ile Asp Val Ser Ser Gln Asp Leu Ser Gly Gln Thr Ala Arg Glu Tyr			
1380	1385	1390	
Ala Val Ser Ser His His His Val Ile Cys Gln Leu Leu Ser Asp Tyr			
1395	1400	1405	
Lys Glu Lys Gln Met Leu Lys Ile Ser Ser Glu Asn Ser Asn Pro Glu			
1410	1415	1420	
Gln Asp Leu Lys Leu Thr Ser Glu Glu Glu Ser Gln Arg Phe Lys Gly			
1425	1430	1435	1440
Ser Glu Asn Ser Gln Pro Glu Lys Met Ser Gln Glu Pro Glu Ile Asn			
1445	1450	1455	
Lys Asp Gly Asp Arg Glu Val Glu Glu Met Lys Lys His Glu Ser			
1460	1465	1470	
Asn Asn Val Gly Leu Leu Glu Asn Leu Thr Asn Gly Val Thr Ala Gly			
1475	1480	1485	
Asn Gly Asp Asn Gly Leu Ile Pro Gln Arg Lys Ser Arg Thr Pro Glu			
1490	1495	1500	
Asn Gln Gln Phe Pro Asp Asn Glu Ser Glu Glu Tyr His Arg Ile Cys			
1505	1510	1515	1520
Glu Leu Val Ser Asp Tyr Lys Glu Lys Gln Met Pro Lys Tyr Ser Ser			
1525	1530	1535	
Glu Asn Ser Asn Pro Glu Gln Asp Leu Lys Leu Thr Ser Glu Glu Glu			
1540	1545	1550	
Ser Gln Arg Leu Glu Gly Ser Glu Asn Gly Gln Pro Glu Lys Arg Ser			
1555	1560	1565	
Gln Glu Pro Glu Ile Asn Lys Asp Gly Asp Arg Glu Leu Glu Asn Phe			
1570	1575	1580	
Met Ala Ile Glu Glu Met Lys Lys His Gly Ser Thr His Val Gly Phe			
1585	1590	1595	1600
Pro Glu Asn Leu Thr Asn Gly Ala Thr Ala Gly Asn Gly Asp Asp Gly			
1605	1610	1615	
Leu Ile Pro Pro Arg Lys Ser Arg Thr Pro Glu Ser Gln Gln Phe Pro			
1620	1625	1630	
Asp Thr Glu Asn Glu Glu Tyr His Ser Asp Glu Gln Asn Asp Thr Gln			
1635	1640	1645	
Lys Gln Phe Cys Glu Glu Gln Asn Thr Gly Ile Leu His Asp Glu Ile			
1650	1655	1660	
Leu Ile His Glu Glu Lys Gln Ile Glu Val Val Glu Lys Met Asn Ser			
1665	1670	1675	1680
Glu Leu Ser Leu Ser Cys Lys Lys Glu Lys Asp Ile Leu His Glu Asn			
1685	1690	1695	
Ser Thr Leu Arg Glu Glu Ile Ala Met Leu Arg Leu Glu Leu Asp Thr			
1700	1705	1710	
Met Lys His Gln Ser Gln Leu			
1715			

<210> 379
 <211> 656
 <212> PRT
 <213> Homo sapien

<400> 379

Met	Val	Val	Glu	Val	Asp	Ser	Met	Pro	Ala	Ala	Ser	Ser	Val	Lys	Lys
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Pro	Phe	Gly	Leu	Arg	Ser	Lys	Met	Gly	Lys	Trp	Cys	Cys	Arg	Cys	Phe
			20					25					30		
Pro	Cys	Cys	Arg	Glu	Ser	Gly	Lys	Ser	Asn	Val	Gly	Thr	Ser	Gly	Asp
		35					40					45			
His	Asp	Asp	Ser	Ala	Met	Lys	Thr	Leu	Arg	Ser	Lys	Met	Gly	Lys	Trp
	50					55					60				
Cys	Arg	His	Cys	Phe	Pro	Cys	Cys	Arg	Gly	Ser	Gly	Lys	Ser	Asn	Val
65					70					75				80	
Gly	Ala	Ser	Gly	Asp	His	Asp	Asp	Ser	Ala	Met	Lys	Thr	Leu	Arg	Asn
			85						90					95	
Lys	Met	Gly	Lys	Trp	Cys	Cys	His	Cys	Phe	Pro	Cys	Cys	Arg	Gly	Ser
			100					105					110		
Gly	Lys	Ser	Lys	Val	Gly	Ala	Trp	Gly	Asp	Tyr	Asp	Asp	Ser	Ala	Phe
		115					120					125			
Met	Glu	Pro	Arg	Tyr	His	Val	Arg	Gly	Glu	Asp	Leu	Asp	Lys	Leu	His
	130					135					140				
Arg	Ala	Ala	Trp	Trp	Gly	Lys	Val	Pro	Arg	Lys	Asp	Leu	Ile	Val	Met
145					150					155				160	
Leu	Arg	Asp	Thr	Asp	Val	Asn	Lys	Lys	Asp	Lys	Gln	Lys	Arg	Thr	Ala
			165						170					175	
Leu	His	Leu	Ala	Ser	Ala	Asn	Gly	Asn	Ser	Glu	Val	Val	Lys	Leu	Leu
		180					185						190		
Leu	Asp	Arg	Arg	Cys	Gln	Leu	Asn	Val	Leu	Asp	Asn	Lys	Lys	Arg	Thr
	195						200					205			
Ala	Leu	Ile	Lys	Ala	Val	Gln	Cys	Gln	Glu	Asp	Glu	Cys	Ala	Leu	Met
	210					215					220				
Leu	Leu	Glu	His	Gly	Thr	Asp	Pro	Asn	Ile	Pro	Asp	Glu	Tyr	Gly	Asn
225					230					235				240	
Thr	Thr	Leu	His	Tyr	Ala	Ile	Tyr	Asn	Glu	Asp	Lys	Leu	Met	Ala	Lys
			245						250					255	
Ala	Leu	Leu	Leu	Tyr	Gly	Ala	Asp	Ile	Glu	Ser	Lys	Asn	Lys	His	Gly
		260					265						270		
Leu	Thr	Pro	Leu	Leu	Leu	Gly	Val	His	Glu	Gln	Lys	Gln	Gln	Val	Val
		275					280						285		
Lys	Phe	Leu	Ile	Lys	Lys	Lys	Ala	Asn	Leu	Asn	Ala	Leu	Asp	Arg	Tyr
	290					295					300				
Gly	Arg	Thr	Ala	Leu	Ile	Leu	Ala	Val	Cys	Cys	Gly	Ser	Ala	Ser	Ile
305					310					315				320	
Val	Ser	Leu	Leu	Leu	Glu	Gln	Asn	Ile	Asp	Val	Ser	Ser	Gln	Asp	Leu
			325						330					335	
Ser	Gly	Gln	Thr	Ala	Arg	Glu	Tyr	Ala	Val	Ser	Ser	His	His	His	Val
			340					345					350		
Ile	Cys	Gln	Leu	Leu	Ser	Asp	Tyr	Lys	Glu	Lys	Gln	Met	Leu	Lys	Ile
		355					360					365			
Ser	Ser	Glu	Asn	Ser	Asn	Pro	Glu	Gln	Asp	Leu	Lys	Leu	Thr	Ser	Glu
	370					375					380				
Glu	Glu	Ser	Gln	Arg	Phe	Lys	Gly	Ser	Glu	Asn	Ser	Gln	Pro	Glu	Lys
385					390					395				400	
Met	Ser	Gln	Glu	Pro	Glu	Ile	Asn	Lys	Asp	Gly	Asp	Arg	Glu	Val	Glu
				405					410					415	

Glu	Glu	Met	Lys	Lys	His	Glu	Ser	Asn	Asn	Val	Gly	Leu	Leu	Glu	Asn
			420					425					430		
Leu	Thr	Asn	Gly	Val	Thr	Ala	Gly	Asn	Gly	Asp	Asn	Gly	Leu	Ile	Pro
		435					440					445			
Gln	Arg	Lys	Ser	Arg	Thr	Pro	Glu	Asn	Gln	Gln	Phe	Pro	Asp	Asn	Glu
		450					455				460				
Ser	Glu	Glu	Tyr	His	Arg	Ile	Cys	Glu	Leu	Val	Ser	Asp	Tyr	Lys	Glu
465					470					475					480
Lys	Gln	Met	Pro	Lys	Tyr	Ser	Ser	Glu	Asn	Ser	Asn	Pro	Glu	Gln	Asp
				485					490					495	
Leu	Lys	Leu	Thr	Ser	Glu	Glu	Glu	Ser	Gln	Arg	Leu	Glu	Gly	Ser	Glu
			500					505					510		
Asn	Gly	Gln	Pro	Glu	Leu	Glu	Asn	Phe	Met	Ala	Ile	Glu	Glu	Met	Lys
		515					520					525			
Lys	His	Gly	Ser	Thr	His	Val	Gly	Phe	Pro	Glu	Asn	Leu	Thr	Asn	Gly
		530				535					540				
Ala	Thr	Ala	Gly	Asn	Gly	Asp	Asp	Gly	Leu	Ile	Pro	Pro	Arg	Lys	Ser
545					550					555					560
Arg	Thr	Pro	Glu	Ser	Gln	Gln	Phe	Pro	Asp	Thr	Glu	Asn	Glu	Glu	Tyr
				565					570					575	
His	Ser	Asp	Glu	Gln	Asn	Asp	Thr	Gln	Lys	Gln	Phe	Cys	Glu	Glu	Gln
			580					585					590		
Asn	Thr	Gly	Ile	Leu	His	Asp	Glu	Ile	Leu	Ile	His	Glu	Glu	Lys	Gln
		595					600					605			
Ile	Glu	Val	Val	Glu	Lys	Met	Asn	Ser	Glu	Leu	Ser	Leu	Ser	Cys	Lys
		610				615					620				
Lys	Glu	Lys	Asp	Ile	Leu	His	Glu	Asn	Ser	Thr	Leu	Arg	Glu	Glu	Ile
625					630					635					640
Ala	Met	Leu	Arg	Leu	Glu	Leu	Asp	Thr	Met	Lys	His	Gln	Ser	Gln	Leu
				645					650						655

<210> 380

<211> 671

<212> PRT

<213> Homo sapien

<400> 380

Met 1	Val	Val	Glu	Val	Asp	Ser	Met	Pro	Ala	Ala	Ser	Ser	Val	Lys	Lys
Pro	Phe	Gly	Leu	Arg	Ser	Lys	Met	Gly	Lys	Trp	Cys	Cys	Arg	Cys	Phe
Pro	Cys	Cys	Arg	Glu	Ser	Gly	Lys	Ser	Asn	Val	Gly	Thr	Ser	Gly	Asp
His	Asp	Asp	Ser	Ala	Met	Lys	Thr	Leu	Arg	Ser	Lys	Met	Gly	Lys	Trp
Cys	Arg	His	Cys	Phe	Pro	Cys	Cys	Arg	Gly	Ser	Gly	Lys	Ser	Asn	Val
Gly	Ala	Ser	Gly	Asp	His	Asp	Asp	Ser	Ala	Met	Lys	Thr	Leu	Arg	Asn
Lys	Met	Gly	Lys	Trp	Cys	Cys	His	Cys	Phe	Pro	Cys	Cys	Arg	Gly	Ser
Gly	Lys	Ser	Lys	Val	Gly	Ala	Trp	Gly	Asp	Tyr	Asp	Asp	Ser	Ala	Phe
Met	Glu	Pro	Arg	Tyr	His	Val	Arg	Gly	Glu	Asp	Leu	Asp	Lys	Leu	His
Arg	Ala	Ala	Trp	Trp	Gly	Lys	Val	Pro	Arg	Lys	Asp	Leu	Ile	Val	Met
Leu	Arg	Asp	Thr	Asp	Val	Asn	Lys	Lys	Asp	Lys	Gln	Lys	Arg	Thr	Ala

625 630 635 640
 Glu Lys Asp Ile Leu His Glu Asn Ser Thr Leu Arg Glu Glu Ile Ala
 645 650 655
 Met Leu Arg Leu Glu Leu Asp Thr Met Lys His Gln Ser Gln Leu
 660 665 670

<210> 381
 <211> 251
 <212> DNA
 <213> Homo sapien

<400> 381
 ggagaagcgt ctgctggggc aggaaggggt ttccctgccc tctcacctgt ccctcaccaa 60
 ggtaacatgc ttcccctaag ggtatcccaa cccagggggc tcacatgac ctctgagggg 120
 ccaatatccc aggagaagca ttggggaggt gggggcaggt gaaggacca ggactcacac 180
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 caagcagtca g 251

<210> 382
 <211> 3279
 <212> DNA
 <213> Homo sapiens

<400> 382
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 cactgggagg ggacatcctg cagaaggtag gagttagcaa acacccgctg caggggaggg 180
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 aagaaggaca gggcctggct cagggtgtcca gaggtgtcg ctggcttccc tttgggatca 480
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gcataatccga cagttattct ctccaagtgg agacttacgg acagcatata attctccctg 2220
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gttttcagac cttaaaaaaa aaaaaaaaaa aaagtgttt 3279

```

<210> 383

<211> 154

<212> PRT

<213> Homo sapiens

<400> 383

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Gly Lys Arg Gly Pro Leu Leu Gln Gly Leu Thr Trp Ala Thr Gly Gly
      20                      25                      30

His Cys Phe Ser Ser Glu Glu Ser Gly Ala Val Asp Gly Ala Gly Gln
      35                      40                      45

Lys Lys Asp Arg Ala Trp Leu Arg Cys Pro Glu Ala Val Ala Gly Phe
      50                      55                      60

Pro Leu Gly Ser Asp Cys Arg Glu Gly Gly Arg Gln Gly Cys Gly Gly
      65                      70                      75                      80

Ser Asp Asp Glu Asp Asp Leu Gly Val Ala Pro Gly Leu Ala Pro Ala
      85                      90                      95

Trp Ala Leu Thr Gln Pro Pro Ser Gln Ser Pro Gly Pro Gln Ser Leu
      100                     105                     110

Pro Ser Thr Pro Ser Ser Ile Trp Pro Gln Trp Val Ile Leu Ile Thr
      115                     120                     125

Glu Leu Thr Ile Pro Ser Pro Ala His Gly Pro Pro Trp Leu Pro Asn
      130                     135                     140

Ala Leu Glu Arg Gly His Leu Val Arg Glu
      145                     150

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<210> 384
<211> 557
<212> DNA
<213> Homo sapiens

<400> 384
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aaagatgtgt tttgttttgg actctctgtg gtcccttcca atgctgtggg ttccaacca 120
ggggaagggt cccttttgca ttgccaagtg ccataaccat gagcactact ctaccatggt 180
tctgcctcct ggccaagcag gctggtttgc aagaatgaaa tgaatgattc tacagctagg 240
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ccttcttatt tatgtgaaca actgtttgtc tttttttgta tcttttttaa actgtaaaagt 480
tcaattgtga aaatgaatat catgcaaaata aattatgcga ttttttttcc aaagtaaaaa 540
aaaaaaaaaa aaaaaaaa 557

<210> 385
<211> 337
<212> DNA
<213> Homo sapiens

<400> 385
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tctcaaagcc atctgctgtc ttcgagtacg gacacatcat cactcctgca ttgttgatca 180
aaacgtggag gtgcttttcc tcagctaaga agcccttagc aaaagctcga atagacttag 240
tatcagacag gtccagtttc cgcaccaaca cctgctggtt ccctgtcgtg gtctggatct 300
ctttggccac caattcccc tttccacat cccggca 337

<210> 386
<211> 300
<212> DNA
<213> Homo sapiens

<400> 386
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gccgcctcgg ccagaggggt gggcgcgggg ctgcctctac cggtggcgg ctgtaactca 120
gcgaccttgg ccgaaggct ctagcaagga ccaccgacc ccagccggc cggcgccggc 180
gcggaacttg ccggtgtgt gggcgggagc ggactgctg tccgcggacg ggcagcgaag 240
atgttagcct tcgctgccag gaccgtggac cgatcccagg gctgtggtgt aacctcagcc 300

<210> 387
<211> 537
<212> DNA
<213> Homo sapiens

<400> 387
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ccccctcctg tgccatcatg atcagcacct atgagttcgg caaaagcttc ttccagaggc 120
tgaaccagga ccggtctctg ggcggctgaa aggggcaagg aggcaaggac ccgctctctc 180
ccacggatgg ggagaggga ggaggagacc cagccaagtg ccttttcctc agcactgagg 240
gagggggcct gtttcccttc cctcccggcg acaagctcca gggcagggtc gtccctctgg 300
gcgcccagc acttctcag acacaacttc ttctgctgc tccagtctg gggatcatca 360
cttaccacc ccccaagttc aagaccaa atctccagctg ccccttcgt gtttccctgt 420
gtttgctgta gctgggcatg tctccaggaa ccaagaagcc ctcagcctgg ttagtctcc 480
ctgacccttg ttaattcctt aagtctaaag atgatgaact tcaaaaaaaaa aaaaaaa 537

<210> 388
 <211> 520
 <212> DNA
 <213> Homo sapiens

<400> 388
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 gtttgaagat tgctcttct acagcttctg agaattgtgt tatttcactt gccaaagtga 180
 ggacccccctc cccaacatgc cccagccac ccctaagcat ggtcccttgt caccaggcaa 240
 ccaggaaact gctacttgtg gacctcacca gagaccagga gggtttggtt agctcacagg 300
 acttccccca cccagaaga ttagcatccc atactagact cataactcaac tcaactaggc 360
 tcataactcaa ttgatgggta ttagacaatt ccatttcttt ctgggttatta taaacagaaa 420
 atctttctctc ttctcattac cagtaaaggc tcttggtatc tttctgttgg aatgatttct 480
 atgaacttgt cttattttaa tgggtgggtt ttttctgtgt 520

<210> 389
 <211> 365
 <212> DNA
 <213> Homo sapiens

<400> 389
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 aacgactttc caaataatct caccagcgcc ttccagctca ggcgtcctag aagcgtcttg 180
 aagcctatgg ccagctgtct ttgtgttccc tctcaccgc ctgtcctcac agctgagact 240
 cccaggaaac cttcagacta ccttcctctg ccttcagcaa ggggcgttgc ccacattctc 300
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 gggag 365

<210> 390
 <211> 221
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> (1) ... (221)
 <223> n = A,T,C or G

<400> 390
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 tacacggnnt ctcattgggtg tggaaacatct ctgcttgagg ttccaggaag gcctctggct 120
 gctctangag tctgancnga ntcgttgccc cantntgaca naaggaaagg cggagcttat 180
 tcaaagtcta gagggagtgg aggagttaag gctggatttc a 221

<210> 391
 <211> 325
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> (1) ... (325)
 <223> n = A,T,C or G

<400> 391

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tggagcaggt cccgaggcct ccctagagcc tggggccgac tctgtgncga tgcangcttt 60
ctctcgcgcc cagcctggag ctgctcctgg catctaccaa caatcagncg aggcgagcag 120
tagccagggc actgctgcca acagccagtc cnnataccat catgtnaccc ggtgngctct 180
naanttngat ntccanagcc ctacccatcn tagttctgct ctcccaccgg ntaccagccc 240
cactgccagc gaatectaca gccagtaccc tgtcccgacg tctctaccta ccagtacgat 300
gagacctccg gctactacta tgacc                                     325

```

<210> 392

<211> 277

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(277)

<223> n = A,T,C or G

<400> 392

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atattgttta actccttcct ttatatcttt taacattttc atggngaaag gttcacatct 60
agtctcactt nggcnagn gn ctctacttg agtctcttcc ccggcctggn ccagtnghaa 120
antaccanga accgncatgn cttanaaact ncctgggttn tgggttnntc aatgactgca 180
tgcaatgcac caccctgtcc actacgtgat gctgtaggat taaagtctca cagtggcgcg 240
ctgaggatag agcgccgctg cctgtgttgc tggggaa                                     277

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<210> 393

<211> 566

<212> DNA

<213> Homo sapiens

<400> 393

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actagtcag tgtggtggaa ttccggcgcc cgtecgacga caggtcagct gtctggctca 60
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ttgccgggaa cactgcagag acaatgctgt gagtttccaa ccttagccca tctgcccggca 180
gagaaggctc agtttgtcca tcagcattat catgatata ggactgggta cttgggttaag 240
gaggggtcta ggagatctgt cctttttaga gacaccttac ttataatgaa gtatttggga 300
gggtggtttt caaaagtaga aatgtcctgt attccgatga tcacccctga aacattttat 360
catttattaa tcacccctgc ctgtgtctat tattatattc atatctctac gctggaaact 420
ttctgcctca atgtttactg tgcctttgtt ttgtctagtt tgtgtgtgtg aaaaaaaaaa 480
cattctctgc ctgagtttta atttttgtcc aaagttattt taatctatac aattaaaagc 540
ttttgcctat caaaaaaaaa aaaaaa                                     566

```

<210> 394

<211> 384

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(384)

<223> n = A,T,C or G

<400> 394

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gcaggaggac cgggctttta ggagttttta gctgagtgct actgtagacc ccaaatacca 180
tcccaagatt atcgggagaa agggggcagc aattacccaa atccggttgg agcatgacgt 240
gaacatccag tttcctgata aggacgatgg gaaccagccc caggacccaa ttaccatcac 300
agggtagcga aagaacacag aagctgccag ggatgctata ctgagaattg tgggtgaact 360

```

tgagcagatg gtttctgagg acgt

384

<210> 395

<211> 399

<212> DNA

<213> Homo sapiens

<400> 395

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tatcagaggt ttcatcattg cggaaattgt ggagtctaag gaaatcatgg cctctgaagt 180
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ccagctactt gtctgcaatt gtatcttcaa gaataccctg gccatccctt tgactgacgt 300
caagtctctt ttggaaagcc tgggcatctc ctactacag acctctgacc atgggacggg 360
gcagcctggt gagaccatcc aatcccaaat aaaatgcac 399
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<210> 396

<211> 403

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(403)

<223> n = A,T,C or G

<400> 396

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gacattttca acttctgtct cagctgtctga taaaacaaat catgtgttta gcttgactcc 120
agacaaggac aacctgttcc ttcataactc tctagagaaa aaaaggagtt gttagtagat 180
actaaaaaaaa gtggatgaat aatctggata ttttccctaa aaagattcct tgaaacacat 240
taggaaaaatg gagggcctta tgatcagaat gctagaatta gtccattgtg ctgaagcagg 300
gttttagggga gggagtggag gataaaaaga ggaaaaaaag aagagtgaga aaacctattt 360
atcaaagcag gtgctatcac tcaatgttag gccctgctct ttt 403
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<210> 397

<211> 100

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(100)

<223> n = A,T,C or G

<400> 397

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tccatccccg ctcttggttg gtnacagaat gactgacaaa 100
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<210> 398

<211> 278

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(278)

<223> n = A,T,C or G

<400> 398
gcgggcgcggt cgacagcaggt tccgccagcg ctcgcccctg ggtgggggatg tgctgcacgc 60
ccacctggac atctggaagt cagcggcctg gatgaaagag cggacttcac ctggggcgat 120
tcactactgt gcctcgacca gtgaggagag ctggaccgac agcgaggtgg actcatcatg 180
ctccgggcag cccatccacc tgtggcagtt cctcaaggag ttgctactca agccccacag 240
ctatggccgc ttcattangt ggctcaacaa ggagaagg 278

<210> 399
<211> 298
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(298)
<223> n = A,T,C or G

<400> 399
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ggggtgccng catggagcgc atgggcgcgg gcctgggcca cggcatggat cgctggggct 120
ccgagatcga gcgcattggg ctggtcatgg accgcatggg ctccgtggag cgcatgggct 180
ccggcattga gcgcattggg ccgctgggccc tcgaccacat ggcctccanc attgancgca 240
tgggccagac catggagcgc attggctctg gcgtggagcn catgggtgcc ggcatggg 298

<210> 400
<211> 548
<212> DNA
<213> Homo sapiens

<400> 400
acatcaacta cttcctcatt ttaaggtatg gcagttccct tcatccccctt ttctgcctt 60
gtacatgtac atgtatgaaa ttctctctc ttaccgaact ctctccacac atcacaagggt 120
caaagaacca caccgttaga agggtaagag ggcaccctat gaaatgaaat ggtgatttct 180
tgagtctctt tttccacgt ttaaggggcc atggcaggac ttagagtgtg gagttaagac 240
tgcagagggc tagagaatta ttccatacag gctttgaggc caccatgtc acttatcccc 300
tataccctct caccatcccc ttgtctactc tgatgcccc aagatgcaac tgggcagcta 360
gttggcccca taattctggg cctttgttgt ttgttttaat tacttgggca tcccaggaag 420
ctttccagt atctcctacc atgggcccc ctctgggat caagcccctc ccaggccctg 480
tccccagccc ctctgcccc agcccaccgg cttgccttgg tgctcagccc tcccattggg 540
agcaggtt 548

<210> 401
<211> 355
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(355)
<223> n = A,T,C or G

<400> 401
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taagagtggg ggcctatttc agctgctttg acaaatgac tggctcctga cttaacgttc 180
tataaatgaa tgtgtgaag caaagtgcc atggtggcgg cgaagaagan aaagatgtgt 240
tttgttttgg actctctgtg gtcccttcca atgctgnggg tttccaacca ggggaagggg 300

cccttttgca ttgccaagtg ccataacccat gagcactact ctaccatggn tctgc 355

<210> 402

<211> 407

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(407)

<223> n = A,T,C or G

<400> 402

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aaatggaaaa cagaaaaaag cagggtgttg actcctactt tctgacaaaa cagactatgc 180
gaataaagat aaaaaagaga aggacattac aaaggtggc ctgaccttg ataatctca 240
ttgcttgata ccaacctggg ctgttttaat tgcccaaacc aaaaggataa tttgctgagg 300
ttgtggagct tctccctgc agagagtccc tgatctccca aaatttggtt gagatgtaag 360
gntgattttg ctgacaactc cttttctgaa gttttactca tttccaa 407

<210> 403

<211> 303

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(303)

<223> n = A,T,C or G

<400> 403

cagtatttat agccnaactg aaaagctagt agcaggcaag tctcaaatcc aggcacccaa 60
tcttaagcaa gagccatggc atggtgaaaa tgcaaaagga gagtctggcc aatctacaaa 120
tagagaacaa gacctactca gtcataaaca aaaaggcaga caccaacatg gatctcatgg 180
gggattggat attgtaatta tagagcagga agatgacagt gatcgtcatt tggcacaaca 240
tcttaacaac gaccgaaacc cattatttac ataaacctcc attcggtaac catgttgaaa 300
gga 303

<210> 404

<211> 225

<212> DNA

<213> Homo sapiens

<400> 404

aagtgttaact tttaaaaatt tagtggattt tgaaaattct tagaggaaag taaaggaaaa 60
attgttaatg cactcattta cctttacatg gtgaaagttc tctcttgatc ctacaaacag 120
acattttcca ctctgttttc catagttggt aagtgtatca gatgtgttgg gcatgtgaat 180
ctccaagtgc ctgtgtaata aataaagtat ctttatttca ttcatt 225

<210> 405

<211> 334

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(334)

<223> n = A,T,C or G

<400> 405

```
gagctgttat actgtgagtt ctactaggaa atcatcaaat ctgaggggtg tctggaggac 60
ttcaatacac ctccccccat agtgaatcag cttccagggg gtccagtcct tctccttact 120
tcatccccat cccatgccaa aggaagaccc tccctccttg gctcacagcc ttctctaggc 180
ttcccagtgct ctccaggaca gagtgggtta tgttttcagc tccatccttg ctgtgagtgt 240
ctggtgcggg tgtgcctcca gcttctgctc agtgcttcat ggacagtgtc cagccccatgt 300
cactctccac tctctcanng tggatcccac ccct 334
```

<210> 406

<211> 216

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(216)

<223> n = A,T,C or G

<400> 406

```
tttcatacct aatgagggag ttganatnac atnnaaccag gaaatgcatg gatctcaang 60
gaaacaaaca cccaataaac tcggagtggc agactgacaa ctgtgagaca tgcacttgct 120
acnaaacaca aatttnatgt tgcacccttg tttctacacc tgtgggttat gacaaagaca 180
actgccaaag aatnttcaag aaggaggact gccant 216
```

<210> 407

<211> 413

<212> DNA

<213> Homo sapiens

<400> 407

```
gctgacttgc tagtatcatc tgcattcatt gaagcacaag aacttcatgc cttgactcat 60
gtaaatgcaa taggattaaa aaataaattt gatatcacat ggaaacagac aaaaaatatt 120
gtacaacatt gcacccagtg tcagattcta cacctggcca ctcaggaagc aagagttaat 180
cccagaggtc tatgtcctaa tgtgttatgg caaatggatg tcatgcacgt accttcattt 240
ggaaaattgt catttgtcca tgtgacagtt gatacttatt cacatttcat atgggcaacc 300
tgccagacag gagaaagtct tcccatgtta aaagacattt attatcttgt tttcctgtca 360
tgggagttcc agaaaaagt taaaacagaca atgggccagg ttctgtagta aag 413
```

<210> 408

<211> 183

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(183)

<223> n = A,T,C or G

<400> 408

```
ggagctngcc ctcaattcct ccatntctat gttancatat ttaatgtctt ttgnnattaa 60
tntttaacta gttaatcctt aaagggctan ntaatcctta actagtccct ccattgtgag 120
cattatcctt ccagtattcn ccttctnttt tatttactcc ttcttggtta cccatgtact 180
ntt 183
```

<210> 409

<211> 250

<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(250)
<223> n = A,T,C or G

<400> 409
cccacgcatg ataagctctt tatttctgta agtcctgcta ggaaatcatc aaatctgacg 60
gtgggttggg ggacctgaac aaacctoctg taattaatca gctttcagtt tctcccccta 120
gtccctcctt caacaacata ggaggatcct ccccttcttt ctgctcacgg ccttatctag 180
gcttcccagt gccccaggga cagcgtgggc tatgtttaca gcgcntcctt gctggggggg 240
ggcctatgc 250

<210> 410
<211> 306
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(306)
<223> n = A,T,C or G

<400> 410
ggctggtttg caagaatgaa atgaatgatt ctacagctag gacttaacct tgaaatggaa 60
agtcttgcaa tcccatattg aggatccgtc tgtgcacatg cctctgtaga gagcagcatt 120
cccaggagacc ttggaaacag ttggcactgt aagggtgctt ctccccaaga cacatcctaa 180
aagggtgttg aatggtgaaa accgcttctt tctttattgc cccttcttat ttatgtgaac 240
nactggttgg ctttttttgn atctttttta aactggaaag ttcaattgng aaaatgaata 300
tcntgc 306

<210> 411
<211> 261
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(261)
<223> n = A,T,C or G

<400> 411
agagatattn cttaggtnaa agttcataga gttcccatga actatatgac tggccacaca 60
ggatcttttg tatttaagga ttctgagatt ttgcttgagc aggattagat aaggctgttc 120
tttaaatgtc tgaaatggaa cagatttcaa aaaaaaaccc cacaatctag ggtgggaaca 180
aggaaggaaa gatgtgaata ggctgatggg caaaaaacca atttaccat cagttccagc 240
cttctctcaa ggngaggcaa a 261

<210> 412
<211> 241
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(241)

<223> n = A,T,C or G

<400> 412

```
ggtcaatggt acctgacatt tctacaacac cccactcacc gatgtattcg ttgcccagtg 60
ggaacatacc agcctgaatt tggaaaaaat aattgtgttt cttgcccagg aaatactacg 120
actgactttg atgggtccac aaacataacc cagtgtaaaa acagaagatg tggaggggag 180
ctgggagatt tctactgggtta cattgaattc ccaaactacc cangcaatta cccagccaac 240
a 241
```

<210> 413

<211> 231

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(231)

<223> n = A,T,C or G

<400> 413

```
aactcttaca atccaagtga ctcactctgtg tgcttgaate ctttccactg tctcatctcc 60
ctcatccaag tttctagtac cttctctttg ttgtgaagga taatcaaact gaacaacaaa 120
aagtttactc tctctatttg gaacctaaaa actctcttct tcttgggtct gagggctcca 180
agaatccttg aatcanttct cagatcattg gggacaccan atcaggaacc t 231
```

<210> 414

<211> 234

<212> DNA

<213> Homo sapiens

<400> 414

```
actgtccatg aagcactgag cagaagctgg aggcacaacg caccagacac tcacagcaag 60
gatggagctg aaaacataac ccactctgtc ctggaggcac tgggaagcct agagaaggct 120
gtgagccaag gagggagggt cttccttttg catgggatgg ggatgaagta aggagaggga 180
ctggaccccc tggaagctga ttcactatgg ggggaggtgt attgaagtcc tcca 234
```

<210> 415

<211> 217

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(217)

<223> n = A,T,C or G

<400> 415

```
gcataggatt aagactgagt atcttttcta cattctttta acttttctaag gggcacttct 60
caaaacacag accaggtagc aaatctccac tgctctaagg ntctcaccac cacttttctca 120
cacctagcaa tagtagaatt cagtcctact tctgaggcca gaagaatggt tcagaaaaat 180
antggattat aaaaaataac aattaagaaa aataatc 217
```

<210> 416

<211> 213

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature
<222> (1)...(213)
<223> n = A,T,C or G

<400> 416
atgcataatnt aaagganact gcctcgcttt tagaagacat ctggncctgct ctctgcatga 60
ggcacagcag taaagctctt tgattcccag aatcaagaac tctccccttc agactattac 120
cgaatgcaag gtgggttaatt gaaggccact aattgatgct caaatagaag gatattgact 180
atattggaac agatggagtc tctactacaa aag 213

<210> 417
<211> 303
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(303)
<223> n = A,T,C or G

<400> 417
nagtcttcag gcccatcagg gaagttcaca ctggagagaa gtcatacata tgtactgtat 60
gtgggaaagg ctttactctg agttcaaate ttcaagccca tcagagagtc cacactggag 120
agaagccata caaatgcaat gagggtggga agagcttcag gagggattcc cattatcaag 180
ttcatctagt ggtccacaca ggagagaaac cctataaatg tgagatatgt ggggaagggct 240
tcantcaaag ttcgtatctt caaatccatc ngaagggncca cagtatanan aaacctttta 300
agt 303

<210> 418
<211> 328
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(328)
<223> n = A,T,C or G

<400> 418
tttttgccgg tgggtggggca gggacggggac angagtctca ctctgttgcc caggctggag 60
tgcacaggca tgatctcggc tctactacaac cctgcctcc catgtccaag cgattcttgt 120
gcctcagcct tccctgtagc tagaattaca ggcacatgcc accacaccca gctagttttt 180
gtatttttag tagagacagg gtttcacat gttggccagg ctggtctcaa actcctnacc 240
tcagnggtca ggctggtctc aaactcctga cctcaagtga tctgcccacc tcagcctccc 300
aaagtgctan gattacaggc cgtgagcc 328

<210> 419
<211> 389
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(389)
<223> n = A,T,C or G

<400> 419
cctcctcaag acggcctgtg gtccgcctcc cggcaaccaa gaagcctgca gtgcatatg 60

```

acccttgagc catggactgg agcctgaaag gcagcgtaca ccctgctcct gatcttgctg 120
cttgtttctt ctctgtggct ccattcatag cacagttggt gactgaggc ttgtgcaggc 180
cgagcaaggc caagctggct caaagagcaa ccagtcaact ctgccacggg gtgccaggca 240
ccggttctcc agccaccaac ctctctcgct cccgcaaagt gcacatcagt tcttctaccc 300
taaaggtagg accaaagggc atctgctttt ctgaagtctt ctgctctatc agccatcacg 360
tggcagccac tcnggctgtg tcgacgcgg 389

```

<210> 420

<211> 408

<212> DNA

<213> Homo sapiens

<400> 420

```

gttcctccta actcctgcca gaaacagctc tcctcaacat gagagctgca cccctcctcc 60
tggccagggc agcaagcctt agccttggct tcttgtttct gcttttttct tggctagacc 120
gaagtgtact agccaaggag ttgaagtttg tgactttggt gtttcggcat ggagaccgaa 180
gtcccattga cacctttccc actgacccca taaaggaatc ctcatggcca caaggatttg 240
gccaaactcac ccagctgggc atggagcagc attatgaact tggagagtat ataagaaaga 300
gatatagaaa attcttgaat gagtctata aacatgaaca ggtttatatt cgaagcacag 360
acgttgaccg gactttgatg aagtgcctatg acaaacctgg caagcccg 408

```

<210> 421

<211> 352

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(352)

<223> n = A,T,C or G

<400> 421

```

gctcaaaaat ctttttactg atnngcatgg ctacacaatc attgactatt acggaggcca 60
gaggagaatg aggcctggcc tgggagccct gtgcctacta naagcacatt agattatcca 120
ttcactgaca gaacaggtct tttttgggtc cttcttctcc accacnata acttgacgtc 180
ctccttcttg aagattcttt ggcagttgtc tttgtcataa cccacaggtg tagaaacaag 240
ggtgcaacat gaaatttctg tttcgtagca agtgcctgtc tcacaagttg gcangtctgc 300
cactccgagt ttattgggtg tttgtttcct ttgagatcca tgcatttctt gg 352

```

<210> 422

<211> 337

<212> DNA

<213> Homo sapiens

<400> 422

```

atgccaccat gctggcaatg cagcgggcgg tcgaaggcct gcatatccag cccaagctgg 60
cgatgatcga cggcaaccgt tgcccgaagt tgccgatgcc agccgaagcg gtggtcaagg 120
gcatagcaa ggtgccggcg atcgcgcgcg cgtcaatcct ggccaaggtc agccgtgatc 180
gtgaaatggc agctgtcgaa ttgatctacc cgggttatgg catcggcggg cataagggtc 240
atccgacacc ggtgcacctg gaagccttgc agcggctggg gccgacgccg attcaccgac 300
gcttcttccg ccggtacggc tggcctatga aaattat 337

```

<210> 423

<211> 310

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature
<222> (1)...(310)
<223> n = A,T,C or G

<400> 423
gctcaaaaat ctttttactg atatggcatg gctacacaat cattgactat tagaggccag 60
aggagaatga ggccctggcct gggagccctg tgccctactan aagcncatta gattatccat 120
tcaactgacag aacaggctctt ttttgggtcc ttcttctcca ccacgatata cttgcagtc 180
tccttcttga agattctttg gcagttgtct ttgtcataac ccacagggtg anaaacaagg 240
gtgcaacatg aaatttctgt ttcgtagcaa gtgcatgtct cacagttgtc aagtctgcc 300
tccgagttta 310

<210> 424
<211> 370
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(370)
<223> n = A,T,C or G

<400> 424
gctcaaaaat ctttttactg ataggcatgg ctacacaatc attgactatt agaggccaga 60
ggagaatgag gcctggcctg ggagccctgt gcctactaga agcacattag attatccatt 120
cactgacaga acaggctctt tttgggtcct tcttctccac cacgatatac ttgcagtcct 180
ccttcttgaa gattcttttg cagttgtctt tgtcataacc cacagggtga gaaacatcct 240
ggttgaatct cctggaactc cctcattagg tatgaaatag catgatgcat tgcataaagt 300
cacgaagggtg gcaaagatca caacgctgcc cagganaaca ttcattgtga taagcaggac 360
tccgtcgacg 370

<210> 425
<211> 216
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(216)
<223> n = A,T,C or G

<400> 425
aattgctatn ntttattttg ccactcaaaa taattaccaa aaaaaaaaaa tnttaaatga 60
taacaacnca acatcaagg n anaanaaca ggaatggntg actntgcata aatnggccga 120
anattatcca ttatnttaag ggttgacttc aggttacagc acacagacaa acatgcccag 180
gaggntntca ggaccgctcg atgtntntg agggagg 216

<210> 426
<211> 596
<212> DNA
<213> Homo sapiens

<400> 426
cttcagtgga ggataaccct gttgccccgg gccgagggtc tccattagga tctgattgat 60
tggcagtcag tgatggaagg gtgttctgat cattccgact gcccgaagg tcgctggcca 120
gctctctgtt ttgctgaggt ggtagtagga cctaatttgt taattaagag tagatgggtga 180
gctgtccttg tattttgatt aacctaattg ccttcccagc acgactcgga ttcagctgga 240
gacatcacgg caacttttaa tgaaatgatt tgaagggccca ttaaggagga cttcccgtta 300

```

ttaggcagtt catctgcact gataacttct tggcagctga gctggctcgga gctgtggccc 360
aaacgcacac ttggcttttg gttttgagat acaactctta atcttttagt catgcttgag 420
ggtggatggc cttttcagct ttaacccaat ttgcaactgcc ttggaagtgt agccaggaga 480
atacactcat atactcgtgg gcttagaggc cacagcagat gtcattggtc tactgcctga 540
gtcccgctgg tcccatccca ggaccttcca tcggcgagta cctgggagcc cgtgct 596

```

<210> 427

<211> 107

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(107)

<223> n = A,T,C or G

<400> 427

```

gaagaattca agttaggttt attcaaaggg cttacngaga atcctanacc caggncccag 60
cccgaggagca gccttanaga gtcctgttt gactgcccgg ctcagng 107

```

<210> 428

<211> 38

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(38)

<223> n = A,T,C or G

<400> 428

```

gaacttcena anaangactt tattcactat tttacatt 38

```

<210> 429

<211> 544

<212> DNA

<213> Homo sapiens

<400> 429

```

ctttgctgga cggaataaaa gtggacgcaa gcatgacctc ctgatgaggg cgctgcattt 60
attgaagagc ggctgcagcc ctgcggttca gattaaaatc cgagaattgt atagacgccg 120
atatccacga actcttgaag gactttctga tttatccaca atcaaatcat cggttttcag 180
tttgatgggt ggctcatcac ctgtagaacc tgacttggcc gtggctggaa tccactcgtt 240
gccttcact tcagttacac ctcactcacc atcctctcct gttggttctg tgctgcttca 300
agatactaag ccacatttg agatgcagca gccatctccc ccaattcctc ctgtccatcc 360
tgatgtgcag ttaaaaaatc tgccctttta tgatgtcctt gatgttctca tcaagcccac 420
gagtttagtt caaagcagta ttcagcgatt tcaagagaag ttttttattt ttgctttgac 480
acctcaacaa gttagagaga tatgcatatc cagggtattt ttgccagggtg gtaggagaga 544
ttat

```

<210> 430

<211> 507

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(507)

<223> n = A,T,C or G

<400> 430

```
cttatacncaa tggggctccc aaacttggtt gtgcagtgga aactccgggg gaattttgaa 60
gaacactgac acccatcttc cccccgaca ctctgattta attgggctgc agtgagaaca 120
gagcatcaat ttaaaaagct gcccagaatg ttntcctggg cagcgttggt atctttgccn 180
ccttcgtgac tttatgcaat gcatcatgct atttcatacc taatgagggg gttccaggag 240
attcaaccag gatgtttcta cncctgtggg ttatgacaaa gacaactgcc aaagaatntt 300
caagaaggag gactgcaagt atatcgtggt ggagaagaag gacccaaaaa agacctgttc 360
tgtcagtgaa tggataatct aatgtgcttc tagtaggcac agggctccca ggccaggcct 420
cattctcttc tggcctctaa tagtcaatga ttgtgtagcc atgcctatca gtaaaaagat 480
ttttgagcaa aaaaaaaaaa aaaaaaa 507
```

<210> 431

<211> 392

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(392)

<223> n = A,T,C or G

<400> 431

```
gaaaattcag aatggataaa aacaaatgaa gtacaaaata tttcagattt acatagcgat 60
aaacaagaaa gcacttatca ggaggactta caaatggaag tacactctan aaccatcatc 120
tatcatggct aaatgtgaga ttagcacagc tgtattatth gtacattgca aacacctaga 180
aagagatggg aaacaaaatc ccaggagttt tgtgtgtgga gtcctgggtt ttccaacaga 240
catcattcca gcattctgag attagggnga ttggggatca ttctggagtt ggaatgttca 300
acaaaagtga tgttggttagg taaaatgtac aacttctgga tctatgcaga cattgaagggt 360
gcaatgagtc tggctttttac tctgctgttt ct 392
```

<210> 432

<211> 387

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(387)

<223> n = A,T,C or G

<400> 432

```
ggtatcanta cataatcaaa tatagctgta gtacatgttt tcattggngt agattaccac 60
aaatgcaagg caacatgtgt agatctcttg tcttattctt ttgtctataa tactgtattg 120
ngtagtccaa gctctcggna gtccagccac tgngaaacat gctcccttta gattaacctc 180
gtggacnctn ttgtgnatt gtctgaactg tagngccctg tattttgctt ctgtctgnga 240
attctgttgc ttctggggca tttccttgng atgcagagga ccaccacaca gatgacagca 300
atctgaattg ntccaatcac agctgcgatt aagacatact gaaatcgtac aggaccggga 360
acaacgtata gaacactgga gtccctt 387
```

<210> 433

<211> 281

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(281)

<223> n = A,T,C or G

<400> 433

```
ttcaactagc anagaanact gcttcagggn gtgtaaaatg aaaggcttcc acgcagttat 60
ctgattaaag aacactaaga gagggacaag gctagaagcc gcaggatgtc tacactatag 120
caggcnctat ttgggttggc tggaggagct gtggaaaaca tggagagatt ggcgctggag 180
atcgccgtgg ctattcctcn ttgntattac accagngagg ntctctgtnt gccactgggt 240
tnnaaaaccg ntatacaata atgatagaat aggacacaca t 281
```

<210> 434

<211> 484

<212> DNA

<213> Homo sapiens

<400> 434

```
ttttaaaata agcatttagt gctcagtcct tactgagtac tctttctctc cctcctcttg 60
aatttaattc tttcaacttg caatttgcaa ggattacaca tttcactgtg atgtatattg 120
tggtgcaaaa aaaaaaaagt gtctttgttt aaaattactt gggttgtaga tccatcttgc 180
tttttcccca ttggaactag tcattaaccc atctctgaac tggtagaaaa acatctgaag 240
agctagtcta tcagcatctg acagggtgaat tggatggttc tcagaacccat ttcacccaga 300
cagcctgttt ctatcctgtt taataaatta gtttgggttc tctacatgca taacaaaccc 360
tgctccaate tgtcacataa aagtctgtga cttgaagttt agtcagcacc cccaccaaac 420
tttatttttc tatgtgtttt ttgcaacata tgagtgtttt gaaaataaag taccatgtgc 480
ttta 484
```

<210> 435

<211> 424

<212> DNA

<213> Homo sapiens

<400> 435

```
gcgccgctca gagcaggtea ctttctgcct tccacgtcct ctttcaagga agccccatgt 60
gggtagcttt caatatcgca gggtcttact cctctgcctc tataagctca aaccaccaa 120
cgatcgggca agtaaacccc ctccctcgcc gacttcggaa ctggcgagag ttcagcgag 180
atgggcctgt ggggaggggg caagatagat gagggggagc ggcatggtgc ggggtgaccc 240
cttgagaga ggaaaaaggc cacaagaggg gctgccaccg ccactaacgg agatggccct 300
ggtagagacc tttgggggtc tggaacctct ggactcccca tgctctaact cccacactct 360
gctatcagaa acttaaaact gaggattttc tctgtttttc actcgcaata aattcagagc 420
aaac 424
```

<210> 436

<211> 667

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(667)

<223> n = A,T,C or G

<400> 436

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accttgggaa nactctcaca atataaaggg tcgtagactt tactccaaat tccaaaaagg 60
tcctggccat gtaatcctga aagttttccc aaggtagcta taaaatcctt ataagggtgc 120
agcctcttct ggaattcctc tgatttcaaa gtctcactct caagttcttg aaaacgaggg 180
cagttcctga aaggcaggta tagcaactga tcttcagaaa gaggaactgt gtgcaccggg 240
atgggctgcc agagtaggat aggattccag atgctgacac cttctggggg aaacagggct 300
gccaggtttg tcatagcact catcaaagtc cggtaacagt ctgtgcttcg aatataaacc 360
```

tggtcatggt tataggactc attcaagaat tttctatata tctttcttat atactctcca 420
agttcataat gctgctccat gccagctgg gtgagttggc caaatccttg tggccatgag 480
gattccttta tggggtcagt gggaaagggt tcaatgggac ttcggtctcc atgccgaaac 540
accaaagtca caaacttcaa ctccctgggt agtacacttc ggtctagcca gaaaaaagc 600
agaacaaga agccaaggct aaggcttgct gccctgccag gaggaggggt gcagctctca 660
tggtgag 667

<210> 437

<211> 693

<212> DNA

<213> Homo sapiens

<400> 437

ctacgtctca accctcattt ttaggtaagg aatcttaagt ccaaagatat taagtgactc 60
acacagccag gtaaggaaag ctggattggc aactaggac tctaccatac cgggttttgt 120
taaagctcag gttaggaggt tgataagctt ggaaggaaact tcagacagct ttttcagatc 180
ataaaagata attcttagcc catgttcttc tccagagcag acctgaaatg acagcacagc 240
agggtactct ctattttcac ccctcttgct tctactctct ggcagtcaga cctgtgggag 300
gccatgggag aaagcagctc tctggatggt tgtacagatc atggactatt ctctgtggac 360
catttctcca ggttacccta ggtgtcacta ttggggggac agccagcatc tttagctttc 420
atttgagttt ctgtctgtct tcagtagagg aaacttttgc tcttcacact tcacatctga 480
acacctaact gctgttgctc ctgaggtggg gaaagacaga tatagagctt acagtattta 540
tcctatttct aggcactgag ggctgtgggg taccttggtg tgccaaaaca gatcctggtt 600
taaggacatg ttgcttcaga gatgtctgta actatctggg ggctctgttg gctctttacc 660
ctgcacatg tgctctcttg gctgaaaatg acc 693

<210> 438

<211> 360

<212> DNA

<213> Homo sapiens

<400> 438

ctgcttatca caatgaatgt tctcctgggc agcgttggtga tctttgccac ctctgtgact 60
ttatgcaatg catcatgcta tttcatacct aatgagggag ttccaggaga ttcaaccagg 120
atgtttctac acctgtgggt tatgacaaag acaactgcc aagaatcttc aagaaggagg 180
actgcaagta tatctggttg agaagaagga cccaaaaaag acctgttctg tcagtgaatg 240
gataatctaa tgtgcttcta gtaggcacag ggctcccagg ccaggcctca ttctcctctg 300
gcctctaata gtcaataatt gtgtagccat gcctatcagt aaaaagattt ttgagcaaac 360

<210> 439

<211> 431

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(431)

<223> n = A,T,C or G

<400> 439

gttctnnta actcctgcc aaacagctc tctcaacat gagagctgca cccctctctc 60
tggccagggc agcaagcctt agccttggct tcttgtttct gcttttttct tggctagacc 120
gaagtgtact agccaaggag ttgaagtttg tgactttggt gtttcggcat ggagaccgaa 180
gtcccattga cacctttccc actgacccca taaaggaatc ctcatggcca caaggatttg 240
gccaactcac ccagctgggc atggagcagc attatgaact tggagagtat ataagaaaga 300
gatatagaaa attcttgaat gagtcctata aacatgaaca ggtttatatt cgaagcacag 360
acgttgaccg gactttgatg agtgctatga caaacctggc agcccgtcga cgcgccgcgc 420
aatttagtag t 431

<210> 440
 <211> 523
 <212> DNA
 <213> Homo sapiens

<400> 440
 agagataaag cttaggtcaa agttcataga gttcccatga actatatgac tggccacaca 60
 ggatcttttg tatttaagga ttctgagatt ttgcttgagc aggattagat aaggctgttc 120
 tttaaatgtc tgaaatggaa cagatttcaa aaaaaaaccc cacaatctag ggtgggaaca 180
 aggaaggaaa gatgtgaata ggctgatggg caaaaaacca atttaccat cagttccagc 240
 cttctctcaa ggagaggcaa agaaaggaga tacagtggag acatctggaa agttttctcc 300
 actggaaaac tgctactatc tgtttttata tttctgttaa aatatatgag gctacagaac 360
 taaaaattaa aacctctttg tgtcccttg tcttggaaac tttatgttcc ttttaaagaa 420
 acaaaaatca aactttacag aaagatttga tgtatgtaac acatatagca gctcttgaag 480
 tatatatatc atagcaaata agtcactctga tgagaacaag cta 523

<210> 441
 <211> 430
 <212> DNA
 <213> Homo sapiens

<400> 441
 gttcctccta actcctgcc aaaaacagctc tcttcaacat gagagctgca cccctcctcc 60
 tggccagggc agcaagcctt agccttggtt tcttgtttct gcttttttcc tggctagacc 120
 gaagtgtact agccaaggag ttgaagtttg tgactttggt gtttcggcat ggagaccgaa 180
 gtccatttga cacttttccc actgacccca taaaggaatc ctcatggcca caaggatttg 240
 gccaactcac ccagctgggc atggagcagc attatgaact tggagagtat ataagaaaga 300
 gatataaaaa attcttgaat gagtcctata aacatgaaca ggtttatatt cgaagcacag 360
 acgttgaccg gactttgatg agtgctatga caaacctggc agcccgtcga cgcggccgcg 420
 aatttagtag 430

<210> 442
 <211> 362
 <212> DNA
 <213> Homo sapiens

<400> 442
 ctaaggaatt agtaggttc ccatcacttg tttggagtgt gctattctaa aagattttga 60
 tttcttggaa tgacaattat attttaactt tgggtgggga aagagttata ggaccacagt 120
 cttcacttct gatacttgta aattaacttt ttattgcact tgttttgacc attaagctat 180
 atgtttagaa atggtcattt tacggaaaaa ttagaaaaat tctgataata gtgcagaata 240
 aatgaattaa tgttttactt aatttatatt gaactgtcaa tgacaaataa aaattctttt 300
 tgattatttt ttgttttcat ttaccagaat aaaaactaag aattaaaagt ttgattacag 360
 tc 362

<210> 443
 <211> 624
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> (1) ... (624)
 <223> n = A,T,C or G

<400> 443
 tttttttttt gcaacacaat atacatcaca gtgaaatgtg taatccttgc aaattgcaag 60

```

ttgaaagaat taaattcaga ggaggggaga gaaagagtac tcagtaggga ctgagcacta 120
aatgcttatt ttaaaagaaa tgtaaagagc agaaagcaat tcaggctacc ctgccttttg 180
tgctggctag tactccggtc ggtgtcagca gcacgtggca ttgaacattg caatgtggag 240
cccaaaccac agaaaatggg gtgaaattgg ccaactttct attaaattgg cttcctgttt 300
tataaaatat tgtgaataat atcacctact tcaaagggca gttatgaggc ttaaatgaac 360
taacgcctac aaaacactta aacatagata acatagggtc aagtactatg tatctggtac 420
atggtaacaa tccttattat taaagtcaac gctaaaatga atgtgtgtgc atatgctaata 480
agtacagaga gagggcactt aaaccaacta agggcctgga ggggaagggtt cctggaaaga 540
ngatgcttgt gctgggtcca aatcttgggtc tactatgacc ttggccaaat tatttaaact 600
ttgtccctat ctgctaaaca gatc 624

```

<210> 444

<211> 425

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1) ... (425)

<223> n = A,T,C or G

<400> 444

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gcacatcatt nntcttgcat tctttgagaa taagaagatc agtaaatagt tcagaagtgg 60
gaagctttgt ccaggcctgt gtgtgaaccc aatgttttgc ttagaaatag aacaagtaag 120
ttcattgcta tagcataaca caaaatttgc ataagtgtg gtcagcaaat ccttgaatgc 180
tgcttaatgt gagaggttgg taaaatcctt tgtgcaacac tctaactccc tgaatgtttt 240
gctgtgctgg gacctgtgca tgccagacaa ggccaagctg gctgaaagag caaccagcca 300
cctctgcaat ctgccacctc ctgctggcag gatttgtttt tgcacacctg gaagagccaa 360
ggaggcacca gggcataagt gagtagactt atggtcgacg cggccgcgaa ttttagtagta 420
gtaga 425

```

<210> 445

<211> 414

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1) ... (414)

<223> n = A,T,C or G

<400> 445

```

catgtttatg nttttggatt actttgggca cctagtgttt ctaaactgct tatcattctt 60
ttctgttttt caaaagcaga gatggccaga gtctcaacaa actgtatctt caagtctttg 120
tgaaattctt tgcattgtgc agattattgg atgtagtctt ctttaactag catataaatc 180
tggtgtgttt cagataaatg aacagcaaaa tgtggtggaa ttaccatttg gaacattgtg 240
aatgaaaaat tgtgtctcta gattatgtaa caaataacta tttcctaacc attgatcttt 300
ggatttttat aatctactc acaaagact aggtctctcc tcttgatttt tgaagcagtg 360
tgggtgctgg attgataaaa aaaaaaaaaa tgcacgcggc cgcgaattta gtatg 414

```

<210> 446

<211> 631

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1) ... (631)

<223> n = A,T,C or G

<400> 446

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acaaattaga anaaagtgcc agagaacacc acataccttg tccggaacat tacaatggct 60
tctgcatgca tgggaagtgt gagcattcta tcaatatgca ggagccatct tgcagggtgtg 120
atgctgggta tactggacaa cactgtgaaa aaaaggacta cagtgttcta tacgttggtc 180
ccggtccctgt acgatttcag tatgtcttaa tgcagctgtg gattggaaca attcagattg 240
ctgtcatctg tgtggtggtc ctctgcatca caagggccaa actttaggta atagcattgg 300
actgagattt gtaaaccttc caaccttcca ggaaatgccc cagaagcaac agaattcaca 360
gacagaagca aaatacaggg cactacagtt cagacaatac aacaagagcg tccacgaggt 420
taatctaaag ggagcatgtt tcacagtggc tggactaccg agagcttggg ctacacaata 480
cagtattata gacaaaagaa taagacaaga gatctacaca tgttgccctg catttggtgt 540
aatctacacc aatgaaaaca tgtactacag ctatatttga ttatgtatgg atatatttga 600
aatagtatac attgtcttga tgtttttct g 631
```

<210> 447

<211> 585

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(585)

<223> n = A,T,C or G

<400> 447

```
ccttgggaaa antntcacia tataaagggt cgtagacttt actccaaatt ccaaaaagggt 60
cctggccatg taatcctgaa agttttccca aggtagctat aaaatcctta taagggtgca 120
gcctcttctg gaattcctct gatttcaaag tctcactctc aagttcttga aaacgagggc 180
agttcctgaa aggcaggtat agcaactgat cttcagaaag aggaactgtg tgcaccggga 240
tgggctgcca gagtaggata ggattccaga tgctgacacc ttctggggga aacagggtctg 300
ccaggtttgt catagcactc atcaaagtcc ggtcaacgtc tgtgcttcga atataaacct 360
gttcattgtt ataggactca ttcaagaatt ttctatatct ctttcttata tactctccaa 420
gttcataatg ctgctccatg cccagctggg tgagttggcc aaatccttgt ggccatgagg 480
attcctttat ggggtcagtg ggaaagggtg caatgggact tcggtctcca tgccgaaaca 540
ccaaagtac aaacttcaac tccttggtca gtacacttcg gtcta 585
```

<210> 448

<211> 93

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(93)

<223> n = A,T,C or G

<400> 448

```
tgctcgtggg tcattctgan nncgaaactg acctgccag ccctgccgan ggccnccat 60
ggctccctag tgccctggag agganggggc tag 93
```

<210> 449

<211> 706

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1) ... (706)

<223> n = A,T,C or G

<400> 449

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ccaagtcat gctntgtgct ggacgctgga caggggggcaa aagcnnttgc tcgtgggtca 60
ttctgancac cgaactgacc atgccagccc tgccgatggt cctccatggc tccctagtgc 120
cctggagagg aggtgtctag tcagagagta gtcctggaag gtggcctctg ngaggagcca 180
cggggacagc atcctgcaga tggtcgggcg cgtccattc gccattcagg ctgcgcaact 240
gttggaagg gcgatcggtg cgggectctt cgtattacg ccagctggcg aaagggggat 300
gtgctgcaag gcgattaagt tgggtaacgc cagggtttcc ccagtcncga cgttgtaaaa 360
cgacggccag tgaattgaat ttaggtgacn ctatagaaga gctatgacgt cgcagtcacg 420
cgtacgtaag cttggatcct ctagagcggc cgcctactac tactaaatc gcggcccgct 480
cgacgtggga tccnactga gagagtggag agtgacatgt gctggacnct gtccatgaag 540
cactgagcag aagctggagg cacaacgcnc cagacactca cagctactca ggaggctgag 600
aacaggttga acctgggagg tggaggttgc aatgagctga gatcaggccn ctgcncacca 660
gcatggatga cagagtgaaa ctccatctta aaaaaaaaaa aaaaaa 706
```

<210> 450

<211> 493

<212> DNA

<213> Homo sapiens

<400> 450

```
gagacggagt gtcactctgt tgcccaggct ggagtgcagc aagacactgt ctaagaaaaa 60
acagttttaa aaggtaaaac aacataaaaa gaaatatact atagtggaaa taagagagtc 120
aaatgaggct gagaacttta caaagggatc ttacagacat gtcgccaata tcaactgcatg 180
agcctaagta taagaacaac ctttggggag aaaccatcat ttgacagtga ggtacaattc 240
caagtcagggt agtgaatgg gtggaattaa actcaaatta atcctgccag ctgaaacgca 300
agagacactg tcagagagtt aaaaagttag ttctatccat gaggtgattc cacagtcttc 360
tcaagtcaac acatctgtga actcacagac caagtcttta aaccactgtt caaactctgc 420
tacacatcag aatcacctgg agagctttac aaactcccat tgccgagggt cgacgcggcc 480
gcgaatttag tag 493
```

<210> 451

<211> 501

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1) ... (501)

<223> n = A,T,C or G

<400> 451

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gggcgcgtcc cattcgccat tcaggctgcg caactgttgg gaaggcgcat cgggtcgggc 60
ctcttcgcta ttacgccagc tggcgaaaagg gggatgtgct gcaaggcgat taagttgggt 120
aacgccaggg ttttcccagt cncgacgttg taaaacgacg gccagtgaat tgaatttagg 180
tgacnctata gaagagctat gacgtcgcat gcacgcgtac gtaagcttgg atcctctaga 240
gcgccgcct actactacta aattcgcgcc cgcgtcgacg tgggatccnc actgagagag 300
tggagagtga catgtgctgg acnctgtcca tgaagcactg agcagaagct ggaggcacia 360
cgcncacagc actcacagct actcaggagg ctgagaacag gttgaacctg ggagggtggag 420
gttgcaatga gctgagatca ggcnctgcn cccagcatg gatgacagag tgaaactcca 480
tcttaaaaaa aaaaaaaaaa a 501
```

<210> 452

<211> 51

<212> DNA

<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(51)
<223> n = A,T,C or G

<400> 452
agacggtttc accnttacaa cnccttttag gatgggnntt ggggagcaag c 51

<210> 453
<211> 317
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(317)
<223> n = A,T,C or G

<400> 453
tacatcttgc tttttcccca ttggaactag tcattaaccc atctctgaac tggtagaaaa 60
acatctgaag agctagtcta tcagcatctg gcaagtgaat tggatggttc tcagaacccat 120
ttcaccana cagcctgttt ctatcctgtt taataaatta gtttgggttc tctacatgca 180
taacaaaccc tgctccaatc tgtcacataa aagtctgtga cttgaagttt antcagcacc 240
cccaccaaac tttatttttc tatgtgtttt ttgcaacata tgagtgtttt gaaaataagg 300
taccatgtc tttatta 317

<210> 454
<211> 231
<212> DNA
<213> Homo sapiens

<400> 454
ttcgaggtag aatcaactct cagagtgtag tttccttcta tagatgagtc agcattaata 60
taagccacgc cagctcttg aaggagtctt gaattctcct ctgctcactc agtagaacca 120
agaagaccaa attcttctgc atcccagctt gcaaacaaaa ttgttcttct aggtctccac 180
ccttcctttt tcagtgttcc aaagctcctc acaatttcat gaacaacagc t 231

<210> 455
<211> 231
<212> DNA
<213> Homo sapiens

<400> 455
taccaaagag ggcataataa tcagtctcac agtagggttc accatcctcc aagtgaaaaa 60
cattgttccg aatgggcttt ccacaggcta cacacacaaa acaggaaaca tgccaagttt 120
gtttcaacgc attgatgact tctccaagga tcttcctttg gcatcgacca cattcagggg 180
caaagaattt ctcatagcac agtcacaat acagggtccc tttctcctct a 231

<210> 456
<211> 231
<212> DNA
<213> Homo sapiens

<400> 456
ttggcaggta cccttacaaa gaagacacca taccttatgc gttattaggt ggaataatca 60
ttccattcag tattatcgtt attattcttg gagaaacctt gtctgtttac tgtaaccttt 120
tgcactcaaa ttcctttatc aggaataact acatagccac tatttacaaa gccattggaa 180

cctttttatt tgggtgcagct gctagtcagct ccttgactga cattgccaag t 231

<210> 457

<211> 231

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(231)

<223> n = A,T,C or G

<400> 457

cgaggtaccc aggggtctga aaatctctnn ttantagtc gatagcaaaa ttgttcatca 60
gcattcctta atatgatctt gctataatta gattttcttc cattagagtt catacagttt 120
tatttgattt tattagcaat ctctttcaga agacccttga gatcattaag ctttgtatcc 180
agttgtctaa atcgatgctt catttcctct gaggtgtcgc tggcttttgt g 231

<210> 458

<211> 231

<212> DNA

<213> Homo sapiens

<400> 458

aggtctgggt cccccactt ccactcccct ctactctctc taggactggg ctgggccaag 60
agaagagggg tggtaggga agcgttgag acctgaagcc ccaccctcta ccttccttca 120
acaccctaac cttgggtaac agcatttgga attatcattt gggatgagta gaatttcaa 180
ggtcctgggt taggcatttt ggggggcccag accccaggag aagaagattc t 231

<210> 459

<211> 231

<212> DNA

<213> Homo sapiens

<400> 459

ggtaccgagg ctgctgaca cagagaaacc ccaacgcgag gaaaggaatg gccagccaca 60
ccttcgcgaa acctgtggtg gccaccagt cctaacggga caggacagag agacagagca 120
gccctgcact gttttccctc caccacagcc atcctgtccc tcattggctc tgtgctttcc 180
actatacaca gtcaccgtcc caatgagaaa caagaaggag caccctccac a 231

<210> 460

<211> 231

<212> DNA

<213> Homo sapiens

<400> 460

gcaggtataa catgctgcaa caacagatgt gactaggaac ggccggtgac atggggaggg 60
cctatcaccc tattcttggg ggctgcttct tcacagtgat catgaagcct agcagcaaat 120
cccacctccc cacacgcaca oggcccagct ggagcccaca gaagggtcct cctgcagcca 180
gtggagcttg gtccagcctc cagtccaccc ctaccaggct taaggataga a 231

<210> 461

<211> 231

<212> DNA

<213> Homo sapiens

<400> 461

cgaggtttga gaagctctaa tgtgcagggg agccgagaag caggcggcct agggaggggtc 60

gcgtgtgctc cagaagagtg tgtgcatgcc agaggggaaa caggcgcttg tgtgtcctgg 120
gtgggggttca gtgaggagtg ggaaattggt tcagcagaac caagccgttg ggtgaataag 180
agggggattc catggcactg atagagccct atagtttcag agctgggaat t 231

<210> 462

<211> 231

<212> DNA

<213> Homo sapiens

<400> 462

aggtaccctc attgtagcca tgggaaaatt gatgttcagt ggggatcagt gaattaaatg 60
gggtcatgca agtataaaaa ttaaaaaaaa aagacttcat gcccaatctc atatgatgtg 120
gaagaactgt tagagagacc aacagggtag tgggttagag atttcagag tcttacattt 180
tctagaggag gtatttaatt tcttctcact catccagtgt tgtatttagg a 231

<210> 463

<211> 231

<212> DNA

<213> Homo sapiens

<400> 463

tactccagcc tggtagacaga gcgagaccct atcacccccc cccacccccc caaaaaaaaa 60
actgagtaga cagggtgtcct cttggcatgg taagtcttaa gtcccctccc agatctgtga 120
catttgacag gtgtcttttc ctctggacct cggtgtcccc atctgagtga gaaaaggcag 180
tggggagggtg gatcttcacg tcgaagcggt atagaagccc gtgtgaaaag c 231

<210> 464

<211> 231

<212> DNA

<213> Homo sapiens

<400> 464

gtactctaag attttatcta agttgccttt tctgggtggg aaagtttaac cttagtgtact 60
aaggacatca catatgaaga atgtttaagt tggagggtggc aacgtgaatt gcaaacaggg 120
cctgtctcag tgactgtgtg cctgtagtcc cagctactcg ggagtctgtg tgaggccagg 180
gggtgccagcg caccagctag atgctctgta acttctaggg cccattttcc c 231

<210> 465

<211> 231

<212> DNA

<213> Homo sapiens

<400> 465

catgttggtg tagctgtggt aatgctggct gcacttcaga cagggttaac ttcagctcct 60
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aggatggcac aatttttggc tgtgttcata atatactcag attagtccag ctccatcaga 180
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<211> 231

<212> DNA

<213> Homo sapiens

<400> 466

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<211> 2229

<212> DNA

<213> Homo sapiens

<400> 469

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2229

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<211> 2426

<212> DNA

<213> Homo sapiens

<400> 470

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<211> 812

<212> DNA

<213> Homo sapiens

<400> 471

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<211> 515

<212> DNA

<213> Homo sapiens

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<400> 472

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<211> 5829

<212> DNA

<213> Homo sapiens

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<210> 474

<211> 1594

<212> DNA

<213> Homo sapiens

<400> 474

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<210> 475

<211> 2414
 <212> DNA
 <213> Homo sapiens

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<400> 475
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 <211> 3434
 <212> DNA
 <213> Homo sapiens

<400> 476

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<210> 477
<211> 140
<212> PRT
<213> Homo sapiens
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His Tyr His Arg Asp Thr Asp Thr Arg Arg His His His Met Asp Thr
      20                      25                      30

Leu Ser His Tyr His Arg Asp Thr Arg His His Thr Val Thr Trp Thr
      35                      40                      45

His His His Thr His Glu His Thr Asp Thr Leu Pro Tyr Gly His Trp
      50                      55                      60

His Thr His Cys His Thr Val Thr Trp Thr His Leu His Thr Ile Thr
      65                      70                      75                      80

Pro Pro His Thr Leu Pro Val Asp Thr Arg Thr His Arg His Cys His
      85                      90                      95

Thr Asp Thr Gln Asn Thr Val Thr Arg Arg His His His Ala Asp Thr
      100                     105                     110

Pro Pro Leu Trp Cys Arg Leu Asn Tyr Pro Ala Gly Gly Thr Ala Val
      115                     120                     125

Ala Tyr Ser Cys Leu Ser Asp Trp Leu Ser Pro Gln
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<210> 478
<211> 143
<212> PRT
<213> Homo sapiens
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Ser His Gly His Thr Gly Ile Val Thr Trp Thr Asp Thr Gln Thr Tyr
      20                      25                      30

Gly Glu Ile Thr Trp Thr His His His Thr Ile Thr Gly Thr Gln Thr
      35                      40                      45

His Gly Asp Ile Thr Thr Trp Thr His Cys His Thr Thr Thr Gly Thr
      50                      55                      60

Arg Asp Ile Thr Leu Ser His Gly His Thr Ile Thr His Met Asn Thr
      65                      70                      75                      80

Pro Thr His Cys His Met Asp Thr Gly Thr His Thr Ala Thr Leu Ser
      85                      90                      95
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His Gly His Thr Ser Thr Pro Ser His His His Thr His Cys Leu Trp
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Thr Gln Gly His Thr Asp Thr Val Thr Gln Ile His Lys Thr Leu Ser
 115 120 125

His Gly Asp Ile Thr Met Gln Ile His His His Ser Gly Ala Val
 130 135 140

<210> 479

<211> 222

<212> PRT

<213> Homo sapiens

<400> 479

Met Tyr Arg His Thr Glu Thr Leu Pro His Gly Asp Thr Val Thr Gln
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Ser His Glu His Thr Gly Ile Val Thr Trp Thr Asp Thr Gln Thr Tyr
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Gly Glu Ile Thr Leu Thr His His His Thr Ile Thr Gly Thr Gln Thr
 35 40 45

His Gly Asp Ile Thr Thr Trp Thr His Cys His Thr Thr Thr Gly Thr
 50 55 60

Arg Asp Ile Thr Leu Ser His Gly His Thr Ile Thr His Met Asn Thr
 65 70 75 80

Pro Thr His Cys His Met Asp Thr Ala Thr His Thr Ala Thr Leu Ser
 85 90 95

His Gly His Thr Ser Ile Pro Ser His His His Thr His Cys His Val
 100 105 110

Asp Thr Arg Thr His Arg His Cys His Thr Asp Thr Gln Asn Thr Val
 115 120 125

Thr Arg Arg His His His Ala Asp Thr Pro Pro His Gly His Ser Thr
 130 135 140

Arg His Ser Ala Thr Gln Ile His His His Thr Glu Met Arg Thr His
 145 150 155 160

Cys His Thr Asp Thr Thr Thr Ser Leu Pro His Phe His Val Ser Ala
 165 170 175

Gly Gly Val Gly Pro Thr Thr Leu Gly Ser Asn Arg Glu Ile Thr Trp
 180 185 190

Thr Tyr Ser Glu Gly Lys Ile Phe Phe Tyr Phe Leu Gly Asn Gln Ala
 195 200 205

Arg Leu Cys Leu Lys Lys Arg Lys Lys Lys Gln Tyr Thr Val
 210 215 220

<210> 480
 <211> 144
 <212> PRT
 <213> Homo sapiens

<400> 480

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Met Glu Pro Tyr Arg Gly Asn Glu Gln Pro Ser Gln Glu Gln Gly Val
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Cys Cys Leu Trp Gly Leu Gln Ser Leu Pro Gln Gly Ser Tyr Val Thr
      20                      25                      30

Val Gly Phe Leu Val Val Lys Arg Gln Thr Ile Gly Arg Leu Glu Arg
      35                      40                      45

Asp Phe Met Phe Lys Cys Arg Lys Gln Pro Gly Leu Pro Pro Ser Gly
      50                      55                      60

Leu Cys Leu Leu Trp Pro Trp Pro Asn Leu Glu Phe Gly Arg Arg Gln
      65                      70                      75                      80

Asp Arg Leu Thr Trp Ser Ser Val Ser Val Ala Gly Val Cys Ala Cys
      85                      90                      95

Arg Ala Arg Pro Gly Trp Leu Gly Glu Gln Pro Ala Thr Ser Ala Gly
      100                     105                     110

Val Arg Leu Glu Gln Val Glu Gln Pro Pro Ala His Pro Leu Gln Glu
      115                     120                     125

Ala Gly Val Ala Arg Phe Pro Arg Pro Glu Trp Val Pro Pro Asn Gly
      130                     135                     140

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<210> 481
 <211> 167
 <212> PRT
 <213> Homo sapiens

<400> 481

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Met His Gly Pro Gln Val Leu Ala Arg Cys Ser Glu Cys Ala Cys Pro
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Ala Leu Ala Ala Thr Ser Ala Gly Val Arg Leu Glu Gly Val Asp Arg
      20                      25                      30

Pro Pro Thr Leu Pro Ser Gln Gly Ser Gly Trp Pro Cys Ser His Ser
      35                      40                      45

Leu Ser Gly Cys His Leu Met Ala Asp Gly Ala Lys Ala Leu Gly Lys
      50                      55                      60

Ala Asp Gly Pro Trp Pro Tyr Leu Phe Val Arg Arg Thr Asp Val Pro

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[illegible]

<210> 482

<211> 143

<212> PRT

<213> Homo sapiens

<400> 482

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			20					25					30		
Arg	Ala	Ser	Trp	Leu	Pro	Gly	Gly	Gly	Pro	Gln	Ala	Ile	Leu	Gly	Arg
		35					40					45			
Thr	Leu	Cys	Ser	Ser	Ala	Glu	Ser	Ser	Gln	Asp	Cys	His	Pro	Gly	Gly
	50					55					60				
Pro	Ser	Ile	Ala	Leu	Ala	Lys	Pro	Cys	Arg	Gly	Val	Trp	Leu	Leu	Phe
65					70					75					80
Glu	Pro	Ala	Trp	Pro	Pro	Trp	His	Ala	Arg	Ala	Pro	Gly	Ala	Gly	Thr
				85					90					95	
Leu	Leu	Arg	Val	Cys	Leu	Ser	Cys	Leu	Gly	Cys	His	Leu	Cys	Gly	Gly
			100					105					110		
Ala	Ser	Gly	Gly	Gly	Gly	Pro	Ala	Thr	Asn	Leu	Thr	Gln	Ser	Arg	Lys
		115					120					125			
Trp	Met	Ala	Met	Phe	Pro	Gln	Pro	Glu	Trp	Leu	Pro	Pro	Asp	Gly	
	130					135					140				

<210> 483

<211> 143

<212> PRT

<213> Homo sapiens

<400> 483

```

Met Glu Thr Gln Arg Gly Asn Lys Gln Arg Ala Gln Glu Gln Gly Val
      5                      10                      15

Cys Cys Leu Trp Gly Ser Ser Pro Cys Leu Gly Ser Tyr Gly Thr Ala
      20                      25                      30

Gly Phe Leu Val Ala Lys Arg Arg Thr Thr Gly Leu Leu Glu Glu Asp
      35                      40                      45

Phe Thr Phe Lys Cys Arg Lys Gln Pro Lys Leu Pro Ser Met Arg Leu
      50                      55                      60

Ser Leu Leu Trp Pro Trp Arg Asp Leu Lys Phe Val Pro Arg Gln Asp
      65                      70                      75                      80

Lys Leu Thr Arg Ser Ser Val Ser Val Ala Gly Ala Tyr Ala Cys Arg
      85                      90                      95

Ala Gly Pro Gly Trp Leu Lys Glu Gln Pro Ala Thr Ser Ala Arg Val
      100                     105                     110

Arg Leu Val Gln Ala Glu His Pro Pro Pro His Pro Leu Glu Glu Val
      115                     120                     125

Gly Met Ala Arg Phe Pro Gln Pro Glu Cys Leu Pro Pro Tyr Cys
      130                     135                     140

```

<210> 484

<211> 30

<212> PRT

<213> Homo Sapien

<400> 484

```

Thr Ala Ala Ser Asp Asn Phe Gln Leu Ser Gln Gly Gly Gln Gly Phe
  1      5                      10                      15
Ala Ile Pro Ile Gly Gln Ala Met Ala Ile Ala Gly Gln Ile
      20                      25                      30

```

<210> 485

<211> 31

<212> DNA

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 485

gggaagctta tcacctatgt gccgcctctg c

31

<210> 486

<211> 27

<212> DNA

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 486

gcgaattctc acgctgagta tttggcc

27

<210> 487

<211> 36

<212> DNA

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 487

cccgaattct tagctgcca tccgaacgcc ttcac

36

<210> 488

<211> 33

<212> DNA

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 488

gggaagcttc ttccccggct gcaccagctg tgc

33

<210> 489

<211> 19

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 489

Met Asp Arg Leu Val Gln Arg Phe Gly Thr Arg Ala Val Tyr Leu Ala
1 5 10 15
Ser Val Ala

<210> 490

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 490

Tyr Leu Ala Ser Val Ala Ala Phe Pro Val Ala Ala Gly Ala Thr Cys
1 5 10 15
Leu Ser His Ser
20

<210> 491

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 491

Thr	Cys	Leu	Ser	His	Ser	Val	Ala	Val	Val	Thr	Ala	Ser	Ala	Ala	Leu
1				5					10					15	
Thr	Gly	Phe	Thr												
			20												

<210> 492

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 492

Ala	Leu	Thr	Gly	Phe	Thr	Phe	Ser	Ala	Leu	Gln	Ile	Leu	Pro	Tyr	Thr
1				5					10					15	
Leu	Ala	Ser	Leu												
			20												

<210> 493

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 493

Tyr	Thr	Leu	Ala	Ser	Leu	Tyr	His	Arg	Glu	Lys	Gln	Val	Phe	Leu	Pro
1				5					10					15	
Lys	Tyr	Arg	Gly												
			20												

<210> 494

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 494

Leu	Pro	Lys	Tyr	Arg	Gly	Asp	Thr	Gly	Gly	Ala	Ser	Ser	Glu	Asp	Ser
1				5					10					15	
Leu	Met	Ile	Ser												
			20												

<210> 495

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 495

Asp Ser Leu Met Thr Ser Phe Leu Pro Gly Pro Lys Pro Gly Ala Pro
1 5 10 15
Phe Pro Asn Gly
20

<210> 496

<211> 21

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 496

Ala Pro Phe Pro Asn Gly His Val Gly Ala Gly Gly Ser Gly Leu Leu
1 5 10 15
Pro Pro Pro Pro Ala
20

<210> 497

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 497

Leu Leu Pro Pro Pro Ala Leu Cys Gly Ala Ser Ala Cys Asp Val
1 5 10 15
Ser Val Arg Val
20

<210> 498

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 498

Asp Val Ser Val Arg Val Val Val Gly Glu Pro Thr Glu Ala Arg Val
1 5 10 15
Val Pro Gly Arg
20

<210> 499

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 499

```
Arg Val Val Pro Gly Arg Gly Ile Cys Leu Asp Leu Ala Ile Leu Asp
 1           5           10           15
Ser Ala Phe Leu
                20
```

<210> 500

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 500

```
Leu Asp Ser Ala Phe Leu Leu Ser Gln Val Ala Pro Ser Leu Phe Met
 1           5           10           15
Gly Ser Ile Val
                20
```

<210> 501

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 501

```
Phe Met Gly Ser Ile Val Gln Leu Ser Gln Ser Val Thr Ala Tyr Met
 1           5           10           15
Val Ser Ala Ala
                20
```

<210> 502

<211> 414

<212> DNA

<213> Homo Sapien

<220>

<221> misc_feature

<222> (1)...(414)

<223> n = A,T,C or G

<400> 502

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tcagtcggtg gaggagtccg ggggtcgcct ggtcacgcct gggacacctt tgacantcac      120
ctgtagagtt tttggaatng acctcagtag caatgcaatg agctgggtcc gccaggctcc      180
aggggaaggg ctggaatgga tcggagccat tgataattgt ccacantacy cgacctgggc      240
gaaaggccga ttnatnattt ccaaaacctn gaccacggtg gatttgaaaa tgaccagtcc      300
gacaaccgag gacacggcca cctatctttg tggcagaatg aatactggta atagtggttg      360
gaagaatatt tggggcccag gcaccctggt caccgtntcc tcagggaac ctaa      414
```

<210> 503

<211> 379

<212> DNA

<213> Homo Sapiens

<220>

<221> misc_feature

<222> (1)...(379)

<223> n = A,T,C or G

<400> 503

atnogatggt gcttgggtcaa aggtgtccag tgtcagtcgg tggaggagtc cgggggtcgc	60
ctggtcacgc ctgggacacc cctgacactc acctgcaccg tntctggatt ngacatcagt	120
agctatggag tgagctgggt ccgccaggct ccagggaagg ggctggnata catcggatca	180
ttagtagtag tggtagattt tacgcgagct gggcgaaagg ccgattcacc atttccaaaa	240
cctngaccac ggtggatttg aaaatcacca gtttgacaac cgaggacacg gccacctatt	300
tntgtgccag agggggggtt aattataaag acatttgggg cccaggcacc ctggtcaccg	360
tntccttagg gcaacctaa	379

<210> 504

<211> 19

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 504

Gly	Phe	Thr	Asn	Tyr	Thr	Asp	Phe	Glu	Asp	Ser	Pro	Tyr	Phe	Lys	Glu
1			5					10					15		
Asn	Ser	Ala													

<210> 505

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 505

Lys	Glu	Asn	Ser	Ala	Phe	Pro	Pro	Phe	Cys	Cys	Asn	Asp	Asn	Val	Thr
1			5					10					15		
Asn	Thr	Ala	Asn												
			20												

<210> 506

<211> 407

<212> DNA

<213> Homo Sapien

<400> 506

atggagacag gcctgcgctg gcttctcctg gtcgctgcgc tcaaagggtg ccagtgtcag	60
tcgctggagg agtcgggggg tcgctgggtc acgcctggga caccctgac actcacctgc	120
accgtctctg gattctccct cagtagcaat gcaatgatct gggtcggcca ggctccaggg	180
aaggggctgg aatacatcg atacattagt tatgggtgta gcgcatacta cgcgagctgg	240
gtgaaaggcc gattcaccat ctccaaaacc tcgaccacgg tggatctgag aatgaccagt	300
ctgacaaccg aggacacggc cacctatttc tgtgccagaa atagtgattt tagtggtatg	360
ttgtggggcc caggcacctt ggtcacgctc tctcagggc aacctaa	407

<210> 507
 <211> 422
 <212> DNA
 <213> Homo Sapien

<400> 507
 atggagacag gcctgcgctg gcttctcctg gtcgctgtgc tcaaagggtg ccagtgtcag 60
 tcggtggagg agtccggggg tcgcctgggc acgcctggga caccctgac actcacctgt 120
 acagtctctg gattctccct cagcaactac gacctgaact gggtcggcca ggctccaggg 180
 aaggggctgg aatggatcgg gatcattaat tatgttggtg ggacggacta cgcgaactgg 240
 gcaaaaggcc gggtcaccat ctccaaaacc tcgaccaccg tggatctcaa gatcgccagt 300
 ccgacaaccg aggacacggc cacctatttc tgtgccagag ggtggaagtg cgatgagtct 360
 ggtccgtgct tgcgcatctg gggcccaggc accctggtca ccgtctcctt agggcaacct 420
 aa 422

<210> 508
 <211> 411
 <212> DNA
 <213> Homo Sapiens

<220>
 <221> misc_feature
 <222> (1)...(411)
 <223> n = A,T,C or G

<400> 508
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 cgggtggagg gtccgggggt cgcctgggtc cgcctgggac acccctgaca ctcacctgca 120
 cagtctctgg aatcgacctc agtagctact gcatgagctg ggtccggcag gctccagggg 180
 aggggctgga atggatcgga atcattggta ctctgggtga cacatactac gcgagggtggg 240
 cgaaaggccg attcaccatc tccaaaacct cgaccacggg gcatntgaaa atcnccagtc 300
 cgacaaccga ggacacggcc acctatttct gtgccagaga tcttcgggat ggtagtagta 360
 ctggttatta taaaatctgg ggcccaggca ccctgggtcac cgtctccttg g 411

<210> 509
 <211> 15
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Made in a lab

<400> 509
 Leu Cys Lys Phe Thr Glu Trp Ile Glu Lys Thr Val Gln Ala Ser
 1 5 10 15

<210> 510
 <211> 15
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Made in a lab

<400> 510
 Pro Glu Tyr Asn Arg Pro Leu Leu Ala Asn Asp Leu Met Leu Ile
 1 5 10 15

<210> 511
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> Made in a lab

<400> 511

Tyr His Pro Ser Met Phe Cys Ala Gly Gly Gly Gln Asp Gln Lys
1 5 10 15

<210> 512
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> Made in a lab

<400> 512

Asp Ser Gly Gly Pro Leu Ile Cys Asn Gly Tyr Leu Gln Gly Leu
1 5 10 15

<210> 513
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> Made in a lab

<400> 513

Ala Pro Cys Gly Gln Val Gly Val Pro Asx Val Tyr Thr Asn Leu
1 5 10 15

<210> 514
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> Made in a lab

<400> 514

Leu Cys Lys Phe Thr Glu Trp Ile Glu Lys Thr Val Gln Ala Ser
1 5 10 15

<210> 515
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> Made in a lab

<400> 515
Met Val Glu Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg
1 5 10 15

<210> 516
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> Made in a lab

<400> 516
Val Ser Glu Ser Asp Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln
1 5 10 15

<210> 517
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> Made in a lab

<400> 517
Glu Val Cys Ser Lys Leu Tyr Asp Pro Leu Tyr His Pro Ser Met
1 5 10 15

<210> 518
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> Made in a lab

<400> 518
Arg Ala Glu Pro Gly Thr Glu Ala Arg Arg His Tyr Asp Glu Gly
1 5 10 15

<210> 519
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> Made in a lab

<400> 519
Arg Ala Glu Pro Gly Thr Glu Ala Arg Arg Asn Tyr Asp Glu Gly Cys
1 5 10 15
Gly

<210> 520
<211> 25
<212> PRT
<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 520

Val	Gly	Glu	Gly	Leu	Tyr	Gln	Gly	Val	Pro	Arg	Ala	Glu	Pro	Gly	Thr
1				5				10					15		
Glu	Ala	Arg	Arg	His	Tyr	Asp	Glu	Gly							
			20				25								

<210> 521

<211> 21

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 521

Ala	Pro	Phe	Pro	Asn	Gly	His	Val	Gly	Ala	Gly	Gly	Ser	Gly	Leu	Leu
1				5				10					15		
Pro	Pro	Pro	Pro	Ala											
				20											

<210> 522

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 522

Leu	Leu	Val	Val	Pro	Ala	Ile	Lys	Lys	Asp	Tyr	Gly	Ser	Gln	Glu	Asp
1				5				10					15		
Phe	Thr	Gln	Val												
			20												

<210> 523

<211> 254

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<220>

<221> VARIANT

<222> (1)...(254)

<223> Xaa = any amino acid

<400> 523

Met	Ala	Thr	Ala	Gly	Asn	Pro	Trp	Gly	Trp	Phe	Leu	Gly	Tyr	Leu	Ile
1				5				10					15		
Leu	Gly	Val	Ala	Gly	Ser	Leu	Val	Ser	Gly	Ser	Cys	Ser	Gln	Ile	Ile
			20				25					30			
Asn	Gly	Glu	Asp	Cys	Ser	Pro	His	Ser	Gln	Pro	Trp	Gln	Ala	Ala	Leu
			35				40					45			

Val Met Glu Asn Glu Leu Phe Cys Ser Gly Val Leu Val His Pro Gln
 50 55 60
 Trp Val Leu Ser Ala Thr His Cys Phe Gln Asn Ser Tyr Thr Ile Gly
 65 70 75 80
 Leu Gly Leu His Ser Leu Glu Ala Asp Gln Glu Pro Gly Ser Gln Met
 85 90 95
 Val Glu Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg Pro Leu
 100 105 110
 Leu Ala Asn Asp Leu Met Leu Ile Lys Leu Asp Glu Ser Val Ser Glu
 115 120 125
 Ser Asp Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln Cys Pro Thr Ala
 130 135 140
 Gly Asn Ser Cys Leu Val Ser Gly Trp Gly Leu Leu Ala Asn Gly Arg
 145 150 155 160
 Met Pro Thr Val Leu Gln Cys Val Asn Val Ser Val Val Ser Glu Glu
 165 170 175
 Val Cys Ser Lys Leu Tyr Asp Pro Leu Tyr His Pro Ser Met Phe Cys
 180 185 190
 Ala Gly Gly Gly Gln Xaa Gln Xaa Asp Ser Cys Asn Gly Asp Ser Gly
 195 200 205
 Gly Pro Leu Ile Cys Asn Gly Tyr Leu Gln Gly Leu Val Ser Phe Gly
 210 215 220
 Lys Ala Pro Cys Gly Gln Val Gly Val Pro Gly Val Tyr Thr Asn Leu
 225 230 235 240
 Cys Lys Phe Thr Glu Trp Ile Glu Lys Thr Val Gln Ala Ser
 245 250

<210> 524

<211> 765

<212> DNA

<213> Homo sapien

<400> 524

atggccacag caggaaatcc ctggggctgg ttccctgggggt acctcatcct tgggtgtcgca 560
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 tcgcagccct ggcaggcggc actggtcatg gaaaacgaat tggtctgctc gggcgctcctg 180
 gtgcacccgc agtgggtgct gtcagccgca cactgtttcc agaactccta caccatcggg 240
 ctgggcctgc acagtcttga ggccgaccaa gagccaggga gccagatggt ggaggccagc 300
 ctctccgtac ggcacccaga gtacaacaga cccttgctcg ctaacgacct catgctcatc 360
 aagttggacg aatccgtgtc cgagtctgac accatccgga gcatcagcat tgcttcgcag 420
 tgccctaccg cggggaactc ttgcctcggt tctggctggg gtctgctggc gaacggcaga 480
 atgcctaccg tgctgcagtg cgtgaacgtg tcggtgggtg ctgaggaggt ctgcagtaag 540
 ctctatgacc cgctgtacca cccagcatg ttctgcgccg gcggagggca agaccagaag 600
 gactcctgca acggtgactc tgggggggcc ctgatctgca acgggtactt gcagggcctt 660
 gtgtctttcg gaaaagcccc gtgtggccaa gttggcgtgc cagggtgtcta caccaacctc 720
 tgcaaatcca ctgagtggat agagaaaacc gtccaggcca gtttaa 765

<210> 525

<211> 254

<212> PRT

<213> Homo sapien

<400> 525

Met Ala Thr Ala Gly Asn Pro Trp Gly Trp Phe Leu Gly Tyr Leu Ile
 1 5 10 15
 Leu Gly Val Ala Gly Ser Leu Val Ser Gly Ser Cys Ser Gln Ile Ile
 20 25 30
 Asn Gly Glu Asp Cys Ser Pro His Ser Gln Pro Trp Gln Ala Ala Leu

180

35	40	45
Val Met Glu Asn Glu Leu Phe Cys Ser Gly Val Leu Val His Pro Gln		
50	55	60
Trp Val Leu Ser Ala Ala His Cys Phe Gln Asn Ser Tyr Thr Ile Gly		
65	70	75
Leu Gly Leu His Ser Leu Glu Ala Asp Gln Glu Pro Gly Ser Gln Met		
85	90	95
Val Glu Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg Pro Leu		
100	105	110
Leu Ala Asn Asp Leu Met Leu Ile Lys Leu Asp Glu Ser Val Ser Glu		
115	120	125
Ser Asp Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln Cys Pro Thr Ala		
130	135	140
Gly Asn Ser Cys Leu Val Ser Gly Trp Gly Leu Leu Ala Asn Gly Arg		
145	150	155
Met Pro Thr Val Leu Gln Cys Val Asn Val Ser Val Val Ser Glu Glu		
165	170	175
Val Cys Ser Lys Leu Tyr Asp Pro Leu Tyr His Pro Ser Met Phe Cys		
180	185	190
Ala Gly Gly Gly Gln Asp Gln Lys Asp Ser Cys Asn Gly Asp Ser Gly		
195	200	205
Gly Pro Leu Ile Cys Asn Gly Tyr Leu Gln Gly Leu Val Ser Phe Gly		
210	215	220
Lys Ala Pro Cys Gly Gln Val Gly Val Pro Gly Val Tyr Thr Asn Leu		
225	230	235
Cys Lys Phe Thr Glu Trp Ile Glu Lys Thr Val Gln Ala Ser		
245	250	

<210> 526

<211> 963

<212> DNA

<213> Homo sapiens

<400> 526

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aactgcacg tggcttcat cgtaaggacg gaacgcagcc tgcacgctcc gatgtacctc 180
tttctctgca tgcttgacg cattgacctg gccttatcca catccaccat gcctaagatc 240
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caggatgtaa tgaagttggc ctatgcagac actttgcccc atgtggtata tggctttact 600
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caccgctttg gaaacagcct tcatccatt gtgcgtgttg tcatgggtga catctacctg 840
ctgtgccttc ctgtcatcaa tcccatcatc tatggtgcc aaaccaaaca gatcagaaca 900
cgggtgctgg ctatgttcaa gatcagctgt gacaaggact tgcaggctgt gggaggcaag 960
tga

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<210> 527

<211> 320

<212> PRT

<213> Homo sapiens

<400> 527

305

310

315

320

<210> 528
<211> 20
<212> DNA
<213> Homo Sapien

<400> 528
actatggtcc agaggctgtg

20

<210> 529
<211> 20
<212> DNA
<213> Homo Sapien

<400> 529
atcacctatg tgccgcctct

20

<210> 530
<211> 1852
<212> DNA
<213> Homo sapiens

<400> 530
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aaaaccacct atgacaagcc cacagccaac ataatactaa atggggaaaa gttagaagca 120
tttctctctga gaactgcaac aataaatata aggatgctgg attttgtcaa atgccttttc 180
tgtgtctgtt gagatgctta tgtgactttg cttttaattc tgtttatgtg attatcacat 240
ttattgactt gctgtgttta gaccggaaga gctgggggtg ttctcaggag ccaccgtgtg 300
ctgoggcagc tcgggataaa cttgaggctg catcactggg gaagaaacac aytctgtgcc 360
gtggcgctga tggctgagga cagagcttca gtgtggcttc tctgcgactg gcttcttcgg 420
ggagtctctc cttcatagt tcatccatag gctccagagg aaaattatat tattttgtta 480
tggatgaaga gtattacgtt gtgcagatat actgcagtgt cttcatctct tgatgtgtga 540
ttgggtaggt tccaccatgt tgccgcagat gacatgattt cagtacctgt gtctggctga 600
aaagtgtttg tttgtgaatg gatattgtgg tttctggatc tcatcctctg tgggtggaca 660
gctttctcca ccttgctgga agtgacctgc tgtccagaag tttgatggct gaggagtata 720
ccatcgtgca ccttctcttc atttctctga tttcttctc cctggatgga cagggggagc 780
ggcaagagca acgtgggcac ttctggagac cacaacgact cctctgtgaa gacgcttggg 840
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aacgtggctg cttggggaga ctacgatgac agcgccttca tggatcccag gtaccacgtc 960
catggagaag atctggacaa gctccacaga gctgcctggg ggggtaaagt cccagaaaag 1020
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Pro Cys Cys Arg Gly Ser Gly Lys Ser Asn Val Val Ala Trp Gly Asp
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 acgctcatgg ggatgtttca gtggtgtggt cgacaaagt ctgaagtga gaatatgatg 3180
 atctcagtag aaagggtcat tgaatacaca gacctgaaa aagaagcacc ttggggaatat 3240
 cagaaacgcc caccaccagc ctggccccat gaaggagtga taatctttga caatgtgaac 3300
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 caagaaaagg ttggcattgt gggaaagaac ggagctggaa aaagtctcct catctcagcc 3420
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 attggaattc acgatttaag gaagaaaatg tcaatcatac ctcaggaacc tgttttgttc 3540
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 aatgccttac aagaggtaca acttaagaa accattgaag atcttctctg taaaaatggat 3660
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 gccagggcaa ttctcaggaa aaatcagata ttgattattg atgaagcgac ggcaaatgtg 3780
 gatccaagaa ctgatgagtt aatacaaaaa aaaatccggg agaaatttgc ccactgcacc 3840
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Met Leu Pro Val Tyr Gln Glu Val Lys Pro Asn Pro Leu Gln Asp Ala
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Asn Leu Cys Ser Arg Val Phe Phe Trp Trp Leu Asn Pro Leu Phe Lys
      20                      25                      30

Ile Gly His Lys Arg Arg Leu Glu Glu Asp Asp Met Tyr Ser Val Leu
      35                      40                      45

Pro Glu Asp Arg Ser Gln His Leu Gly Glu Glu Leu Gln Gly Phe Trp
      50                      55                      60

Asp Lys Glu Val Leu Arg Ala Glu Asn Asp Ala Gln Lys Pro Ser Leu

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65		70		75		80
Thr Arg Ala Ile	Ile Lys Cys Tyr Trp	Lys Ser Tyr Leu Val	Leu Gly			
	85	90	95			
Ile Phe Thr Leu	Ile Glu Glu Ser Ala Lys Val	Ile Gln Pro Ile Phe				
	100	105	110			
Leu Gly Lys Ile	Ile Asn Tyr Phe Glu Asn Tyr Asp	Pro Met Asp Ser				
	115	120	125			
Val Ala Leu Asn Thr	Ala Tyr Ala Tyr Ala Thr	Val Leu Thr Phe Cys				
	130	135	140			
Thr Leu Ile Leu Ala	Ile Leu His His Leu Tyr Phe Tyr His Val Gln					
	145	150	155			160
Cys Ala Gly Met Arg	Leu Arg Val Ala Met Cys His Met Ile Tyr Arg					
	165	170	175			
Lys Ala Leu Arg	Leu Ser Asn Met Ala Met Gly Lys Thr Thr Thr Gly					
	180	185	190			
Gln Ile Val Asn Leu	Leu Ser Asn Asp Val Asn Lys Phe Asp Gln Val					
	195	200	205			
Thr Val Phe Leu His	Phe Leu Trp Ala Gly Pro Leu Gln Ala Ile Ala					
	210	215	220			
Val Thr Ala Leu Leu	Trp Met Glu Ile Gly Ile Ser Cys Leu Ala Gly					
	225	230	235			240
Met Ala Val Leu Ile	Ile Leu Leu Pro Leu Gln Ser Cys Phe Gly Lys					
	245	250	255			
Leu Phe Ser Ser Leu	Arg Ser Lys Thr Ala Thr Phe Thr Asp Ala Arg					
	260	265	270			
Ile Arg Thr Met Asn	Glu Val Ile Thr Gly Ile Arg Ile Ile Lys Met					
	275	280	285			
Tyr Ala Trp Glu Lys	Ser Phe Ser Asn Leu Ile Thr Asn Leu Arg Lys					
	290	295	300			
Lys Glu Ile Ser Lys	Ile Leu Arg Ser Ser Cys Leu Arg Gly Met Asn					
	305	310	315			320
Leu Ala Ser Phe Phe	Ser Ala Ser Lys Ile Ile Val Phe Val Thr Phe					
	325	330	335			
Thr Thr Tyr Val Leu	Leu Gly Ser Val Ile Thr Ala Ser Arg Val Phe					
	340	345	350			
Val Ala Val Thr Leu	Tyr Gly Ala Val Arg Leu Thr Val Thr Leu Phe					
	355	360	365			
Phe Pro Ser Ala Ile	Glu Arg Val Ser Glu Ala Ile Val Ser Ile Arg					
	370	375	380			

Arg Ile Gln Thr Phe Leu Leu Leu Asp Glu Ile Ser Gln Arg Asn Arg
 385 390 395 400
 Gln Leu Pro Ser Asp Gly Lys Lys Met Val His Val Gln Asp Phe Thr
 405 410 415
 Ala Phe Trp Asp Lys Ala Ser Glu Thr Pro Thr Leu Gln Gly Leu Ser
 420 425 430
 Phe Thr Val Arg Pro Gly Glu Leu Leu Ala Val Val Gly Pro Val Gly
 435 440 445
 Ala Gly Lys Ser Ser Leu Leu Ser Ala Val Leu Gly Glu Leu Ala Pro
 450 455 460
 Ser His Gly Leu Val Ser Val His Gly Arg Ile Ala Tyr Val Ser Gln
 465 470 475 480
 Gln Pro Trp Val Phe Ser Gly Thr Leu Arg Ser Asn Ile Leu Phe Gly
 485 490 495
 Lys Lys Tyr Glu Lys Glu Arg Tyr Glu Lys Val Ile Lys Ala Cys Ala
 500 505 510
 Leu Lys Lys Asp Leu Gln Leu Leu Glu Asp Gly Asp Leu Thr Val Ile
 515 520 525
 Gly Asp Arg Gly Thr Thr Leu Ser Gly Gly Gln Lys Ala Arg Val Asn
 530 535 540
 Leu Ala Arg Ala Val Tyr Gln Asp Ala Asp Ile Tyr Leu Leu Asp Asp
 545 550 555 560
 Pro Leu Ser Ala Val Asp Ala Glu Val Ser Arg His Leu Phe Glu Leu
 565 570 575
 Cys Ile Cys Gln Ile Leu His Glu Lys Ile Thr Ile Leu Val Thr His
 580 585 590
 Gln Leu Gln Tyr Leu Lys Ala Ala Ser Gln Ile Leu Ile Leu Lys Asp
 595 600 605
 Gly Lys Met Val Gln Lys Gly Thr Tyr Thr Glu Phe Leu Lys Ser Gly
 610 615 620
 Ile Asp Phe Gly Ser Leu Leu Lys Lys Asp Asn Glu Glu Ser Glu Gln
 625 630 635 640
 Pro Pro Val Pro Gly Thr Pro Thr Leu Arg Asn Arg Thr Phe Ser Glu
 645 650 655
 Ser Ser Val Trp Ser Gln Gln Ser Ser Arg Pro Ser Leu Lys Asp Gly
 660 665 670
 Ala Leu Glu Ser Gln Asp Thr Glu Asn Val Pro Val Thr Leu Ser Glu
 675 680 685

Glu Asn Arg Ser Glu Gly Lys Val Gly Phe Gln Ala Tyr Lys Asn Tyr
 690 695 700
 Phe Arg Ala Gly Ala His Trp Ile Val Phe Ile Phe Leu Ile Leu Leu
 705 710 715 720
 Asn Thr Ala Ala Gln Val Ala Tyr Val Leu Gln Asp Trp Trp Leu Ser
 725 730 735
 Tyr Trp Ala Asn Lys Gln Ser Met Leu Asn Val Thr Val Asn Gly Gly
 740 745 750
 Gly Asn Val Thr Glu Lys Leu Asp Leu Asn Trp Tyr Leu Gly Ile Tyr
 755 760 765
 Ser Gly Leu Thr Val Ala Thr Val Leu Phe Gly Ile Ala Arg Ser Leu
 770 775 780
 Leu Val Phe Tyr Val Leu Val Asn Ser Ser Gln Thr Leu His Asn Lys
 785 790 795 800
 Met Phe Glu Ser Ile Leu Lys Ala Pro Val Leu Phe Phe Asp Arg Asn
 805 810 815
 Pro Ile Gly Arg Ile Leu Asn Arg Phe Ser Lys Asp Ile Gly His Leu
 820 825 830
 Asp Asp Leu Leu Pro Leu Thr Phe Leu Asp Phe Ile Gln Thr Leu Leu
 835 840 845
 Gln Val Val Gly Val Val Ser Val Ala Val Ala Val Ile Pro Trp Ile
 850 855 860
 Ala Ile Pro Leu Val Pro Leu Gly Ile Ile Phe Ile Phe Leu Arg Arg
 865 870 875 880
 Tyr Phe Leu Glu Thr Ser Arg Asp Val Lys Arg Leu Glu Ser Thr Thr
 885 890 895
 Arg Ser Pro Val Phe Ser His Leu Ser Ser Ser Leu Gln Gly Leu Trp
 900 905 910
 Thr Ile Arg Ala Tyr Lys Ala Glu Glu Arg Cys Gln Glu Leu Phe Asp
 915 920 925
 Ala His Gln Asp Leu His Ser Glu Ala Trp Phe Leu Phe Leu Thr Thr
 930 935 940
 Ser Arg Trp Phe Ala Val Arg Leu Asp Ala Ile Cys Ala Met Phe Val
 945 950 955 960
 Ile Ile Val Ala Phe Gly Ser Leu Ile Leu Ala Lys Thr Leu Asp Ala
 965 970 975
 Gly Gln Val Gly Leu Ala Leu Ser Tyr Ala Leu Thr Leu Met Gly Met
 980 985 990
 Phe Gln Trp Cys Val Arg Gln Ser Ala Glu Val Glu Asn Met Met Ile

995 1000 1005
 Ser Val Glu Arg Val Ile Glu Tyr Thr Asp Leu Glu Lys Glu Ala Pro
 1010 1015 1020
 Trp Glu Tyr Gln Lys Arg Pro Pro Pro Ala Trp Pro His Glu Gly Val
 1025 1030 1035 1040
 Ile Ile Phe Asp Asn Val Asn Phe Met Tyr Ser Pro Gly Gly Pro Leu
 1045 1050 1055
 Val Leu Lys His Leu Thr Ala Leu Ile Lys Ser Gln Glu Lys Val Gly
 1060 1065 1070
 Ile Val Gly Arg Thr Gly Ala Gly Lys Ser Ser Leu Ile Ser Ala Leu
 1075 1080 1085
 Phe Arg Leu Ser Glu Pro Glu Gly Lys Ile Trp Ile Asp Lys Ile Leu
 1090 1095 1100
 Thr Thr Glu Ile Gly Leu His Asp Leu Arg Lys Lys Met Ser Ile Ile
 1105 1110 1115 1120
 Pro Gln Glu Pro Val Leu Phe Thr Gly Thr Met Arg Lys Asn Leu Asp
 1125 1130 1135
 Pro Phe Asn Glu His Thr Asp Glu Glu Leu Trp Asn Ala Leu Gln Glu
 1140 1145 1150
 Val Gln Leu Lys Glu Thr Ile Glu Asp Leu Pro Gly Lys Met Asp Thr
 1155 1160 1165
 Glu Leu Ala Glu Ser Gly Ser Asn Phe Ser Val Gly Gln Arg Gln Leu
 1170 1175 1180
 Val Cys Leu Ala Arg Ala Ile Leu Arg Lys Asn Gln Ile Leu Ile Ile
 1185 1190 1195 1200
 Asp Glu Ala Thr Ala Asn Val Asp Pro Arg Thr Asp Glu Leu Ile Gln
 1205 1210 1215
 Lys Lys Ser Gly Arg Asn Leu Pro Thr Ala Pro Cys
 1220 1225

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 <212> PRT
 <213> Homo sapiens

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 Met Tyr Ser Val Leu Pro Glu Asp Arg Ser Gln His Leu Gly Glu Glu
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 Leu Gln Gly Phe Trp Asp Lys Glu Val Leu Arg Ala Glu Asn Asp Ala
 20 25 30
 Gln Lys Pro Ser Leu Thr Arg Ala Ile Ile Lys Cys Tyr Trp Lys Ser
 35 40 45

Tyr Leu Val Leu Gly Ile Phe Thr Leu Ile Glu Glu Ser Ala Lys Val
 50 55 60
 Ile Gln Pro Ile Phe Leu Gly Lys Ile Ile Asn Tyr Phe Glu Asn Tyr
 65 70 75 80
 Asp Pro Met Asp Ser Val Ala Leu Asn Thr Ala Tyr Ala Tyr Ala Thr
 85 90 95
 Val Leu Thr Phe Cys Thr Leu Ile Leu Ala Ile Leu His His Leu Tyr
 100 105 110
 Phe Tyr His Val Gln Cys Ala Gly Met Arg Leu Arg Val Ala Met Cys
 115 120 125
 His Met Ile Tyr Arg Lys Ala Leu Arg Leu Ser Asn Met Ala Met Gly
 130 135 140
 Lys Thr Thr Thr Gly Gln Ile Val Asn Leu Leu Ser Asn Asp Val Asn
 145 150 155 160
 Lys Phe Asp Gln Val Thr Val Phe Leu His Phe Leu Trp Ala Gly Pro
 165 170 175
 Leu Gln Ala Ile Ala Val Thr Ala Leu Leu Trp Met Glu Ile Gly Ile
 180 185 190
 Ser Cys Leu Ala Gly Met Ala Val Leu Ile Ile Leu Leu Pro Leu Gln
 195 200 205
 Ser Cys Phe Gly Lys Leu Phe Ser Ser Leu Arg Ser Lys Thr Ala Thr
 210 215 220
 Phe Thr Asp Ala Arg Ile Arg Thr Met Asn Glu Val Ile Thr Gly Ile
 225 230 235 240
 Arg Ile Ile Lys Met Tyr Ala Trp Glu Lys Ser Phe Ser Asn Leu Ile
 245 250 255
 Thr Asn Leu Arg Lys Lys Glu Ile Ser Lys Ile Leu Arg Ser Ser Cys
 260 265 270
 Leu Arg Gly Met Asn Leu Ala Ser Phe Phe Ser Ala Ser Lys Ile Ile
 275 280 285
 Val Phe Val Thr Phe Thr Thr Tyr Val Leu Leu Gly Ser Val Ile Thr
 290 295 300
 Ala Ser Arg Val Phe Val Ala Val Thr Leu Tyr Gly Ala Val Arg Leu
 305 310 315 320
 Thr Val Thr Leu Phe Phe Pro Ser Ala Ile Glu Arg Val Ser Glu Ala
 325 330 335
 Ile Val Ser Ile Arg Arg Ile Gln Thr Phe Leu Leu Leu Asp Glu Ile
 340 345 350

Ser Gln Arg Asn Arg Gln Leu Pro Ser Asp Gly Lys Lys Met Val His
 355 360 365
 Val Gln Asp Phe Thr Ala Phe Trp Asp Lys Ala Ser Glu Thr Pro Thr
 370 375 380
 Leu Gln Gly Leu Ser Phe Thr Val Arg Pro Gly Glu Leu Leu Ala Val
 385 390 395 400
 Val Gly Pro Val Gly Ala Gly Lys Ser Ser Leu Leu Ser Ala Val Leu
 405 410 415
 Gly Glu Leu Ala Pro Ser His Gly Leu Val Ser Val His Gly Arg Ile
 420 425 430
 Ala Tyr Val Ser Gln Gln Pro Trp Val Phe Ser Gly Thr Leu Arg Ser
 435 440 445
 Asn Ile Leu Phe Gly Lys Lys Tyr Glu Lys Glu Arg Tyr Glu Lys Val
 450 455 460
 Ile Lys Ala Cys Ala Leu Lys Lys Asp Leu Gln Leu Leu Glu Asp Gly
 465 470 475 480
 Asp Leu Thr Val Ile Gly Asp Arg Gly Thr Thr Leu Ser Gly Gly Gln
 485 490 495
 Lys Ala Arg Val Asn Leu Ala Arg Ala Val Tyr Gln Asp Ala Asp Ile
 500 505 510
 Tyr Leu Leu Asp Asp Pro Leu Ser Ala Val Asp Ala Glu Val Ser Arg
 515 520 525
 His Leu Phe Glu Leu Cys Ile Cys Gln Ile Leu His Glu Lys Ile Thr
 530 535 540
 Ile Leu Val Thr His Gln Leu Gln Tyr Leu Lys Ala Ala Ser Gln Ile
 545 550 555 560
 Leu Ile Leu Lys Asp Gly Lys Met Val Gln Lys Gly Thr Tyr Thr Glu
 565 570 575
 Phe Leu Lys Ser Gly Ile Asp Phe Gly Ser Leu Leu Lys Lys Asp Asn
 580 585 590
 Glu Glu Ser Glu Gln Pro Pro Val Pro Gly Thr Pro Thr Leu Arg Asn
 595 600 605
 Arg Thr Phe Ser Glu Ser Ser Val Trp Ser Gln Gln Ser Ser Arg Pro
 610 615 620
 Ser Leu Lys Asp Gly Ala Leu Glu Ser Gln Asp Thr Glu Asn Val Pro
 625 630 635 640
 Val Thr Leu Ser Glu Glu Asn Arg Ser Glu Gly Lys Val Gly Phe Gln
 645 650 655
 Ala Tyr Lys Asn Tyr Phe Arg Ala Gly Ala His Trp Ile Val Phe Ile

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Phe	Leu	Ile	Leu	Leu	Asn	Thr	Ala	Ala	Gln	Val	Ala	Tyr	Val	Leu	Gln	
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Thr	Val	Asn	Gly	Gly	Gly	Asn	Val	Thr	Glu	Lys	Leu	Asp	Leu	Asn	Trp	
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Tyr	Leu	Gly	Ile	Tyr	Ser	Gly	Leu	Thr	Val	Ala	Thr	Val	Leu	Phe	Gly	
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Ile	Ala	Arg	Ser	Leu	Leu	Val	Phe	Tyr	Val	Leu	Val	Asn	Ser	Ser	Gln	
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Thr	Leu	His	Asn	Lys	Met	Phe	Glu	Ser	Ile	Leu	Lys	Ala	Pro	Val	Leu	
755					760					765						
Phe	Phe	Asp	Arg	Asn	Pro	Ile	Gly	Arg	Ile	Leu	Asn	Arg	Phe	Ser	Lys	
770					775					780						
Asp	Ile	Gly	His	Leu	Asp	Asp	Leu	Leu	Pro	Leu	Thr	Phe	Leu	Asp	Phe	
785					790					795					800	
Ile	Gln	Thr	Leu	Leu	Gln	Val	Val	Gly	Val	Val	Ser	Val	Ala	Val	Ala	
805					810					815						
Val	Ile	Pro	Trp	Ile	Ala	Ile	Pro	Leu	Val	Pro	Leu	Gly	Ile	Ile	Phe	
820					825					830						
Ile	Phe	Leu	Arg	Arg	Tyr	Phe	Leu	Glu	Thr	Ser	Arg	Asp	Val	Lys	Arg	
835					840					845						
Leu	Glu	Ser	Thr	Thr	Arg	Ser	Pro	Val	Phe	Ser	His	Leu	Ser	Ser	Ser	
850					855					860						
Leu	Gln	Gly	Leu	Trp	Thr	Ile	Arg	Ala	Tyr	Lys	Ala	Glu	Glu	Arg	Cys	
865					870					875					880	
Gln	Glu	Leu	Phe	Asp	Ala	His	Gln	Asp	Leu	His	Ser	Glu	Ala	Trp	Phe	
885					890					895						
Leu	Phe	Leu	Thr	Thr	Ser	Arg	Trp	Phe	Ala	Val	Arg	Leu	Asp	Ala	Ile	
900					905					910						
Cys	Ala	Met	Phe	Val	Ile	Ile	Val	Ala	Phe	Gly	Ser	Leu	Ile	Leu	Ala	
915					920					925						
Lys	Thr	Leu	Asp	Ala	Gly	Gln	Val	Gly	Leu	Ala	Leu	Ser	Tyr	Ala	Leu	
930					935					940						
Thr	Leu	Met	Gly	Met	Phe	Gln	Trp	Cys	Val	Arg	Gln	Ser	Ala	Glu	Val	
945					950					955					960	
Glu	Asn	Met	Met	Ile	Ser	Val	Glu	Arg	Val	Ile	Glu	Tyr	Thr	Asp	Leu	
965					970					975						

Glu Lys Glu Ala Pro Trp Glu Tyr Gln Lys Arg Pro Pro Pro Ala Trp
 980 985 990
 Pro His Glu Gly Val Ile Ile Phe Asp Asn Val Asn Phe Met Tyr Ser
 995 1000 1005
 Pro Gly Gly Pro Leu Val Leu Lys His Leu Thr Ala Leu Ile Lys Ser
 1010 1015 1020
 Gln Glu Lys Val Gly Ile Val Gly Arg Thr Gly Ala Gly Lys Ser Ser
 1025 1030 1035 1040
 Leu Ile Ser Ala Leu Phe Arg Leu Ser Glu Pro Glu Gly Lys Ile Trp
 1045 1050 1055
 Ile Asp Lys Ile Leu Thr Thr Glu Ile Gly Leu His Asp Leu Arg Lys
 1060 1065 1070
 Lys Met Ser Ile Ile Pro Gln Glu Pro Val Leu Phe Thr Gly Thr Met
 1075 1080 1085
 Arg Lys Asn Leu Asp Pro Phe Asn Glu His Thr Asp Glu Glu Leu Trp
 1090 1095 1100
 Asn Ala Leu Gln Glu Val Gln Leu Lys Glu Thr Ile Glu Asp Leu Pro
 1105 1110 1115 1120
 Gly Lys Met Asp Thr Glu Leu Ala Glu Ser Gly Ser Asn Phe Ser Val
 1125 1130 1135
 Gly Gln Arg Gln Leu Val Cys Leu Ala Arg Ala Ile Leu Arg Lys Asn
 1140 1145 1150
 Gln Ile Leu Ile Ile Asp Glu Ala Thr Ala Asn Val Asp Pro Arg Thr
 1155 1160 1165
 Asp Glu Leu Ile Gln Lys Lys Ile Arg Glu Lys Phe Ala His Cys Thr
 1170 1175 1180
 Val Leu Thr Ile Ala His Arg Leu Asn Thr Ile Ile Asp Ser Asp Lys
 1185 1190 1195 1200
 Ile Met Val Leu Asp Ser Gly Arg Leu Lys Glu Tyr Asp Glu Pro Tyr
 1205 1210 1215
 Val Leu Leu Gln Asn Lys Glu Ser Leu Phe Tyr Lys Met Val Gln Gln
 1220 1225 1230
 Leu Gly Lys Ala Glu Ala Ala Ala Leu Thr Glu Thr Ala Lys Gln Arg
 1235 1240 1245
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<213> Artificial Sequence

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<223> Made in a lab

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<212> PRT

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<223> Made in a lab

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<211> 14

<212> PRT

<213> Homo sapiens

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<210> 542

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<212> PRT

<213> Homo sapiens

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<211> 12

<212> PRT

<213> Homo sapiens

<400> 543

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<211> 18

<212> PRT

<213> Homo sapiens

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Met Thr

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<211> 18

<212> PRT

<213> Homo sapiens

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10

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Ser Val

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<211> 29

<212> PRT

<213> Homo sapiens

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Phe Val Gly Glu Gly Leu Tyr Gln Gly Val Pro Arg Ala Glu Pro Gly

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Thr Glu Ala Arg Arg His Tyr Asp Glu Gly Val Arg Met

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25

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<211> 58

<212> PRT

<213> Homo sapiens

<400> 547

Val Ala Glu Glu Ala Ala Leu Gly Pro Thr Glu Pro Ala Glu Gly Leu

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15

Ser Ala Pro Ser Leu Ser Pro His Cys Cys Pro Cys Arg Ala Arg Leu

20

25

30

Ala Phe Arg Asn Leu Gly Ala Leu Leu Pro Arg Leu His Gln Leu Cys

35

40

45

Cys Arg Met Pro Arg Thr Leu Arg Arg Leu

50

55

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<211> 18

<212> PRT

<213> Homo sapiens

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Ile Asp Trp Asp Thr Ser Ala Leu Ala Pro Tyr Leu Gly Thr Gln Glu

200

5

10

15

Glu Cys

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<211> 18

<212> PRT

<213> Homo sapiens

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Leu Glu Ala Leu Leu Ser Asp Leu Phe Arg Asp Pro Asp His Cys Arg

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10

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Gln Ala

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<212> PRT

<213> Homo sapiens

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Ser Asp His Trp Arg Gly Arg Tyr Gly Arg Arg Arg Pro Phe

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<210> 551

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<212> PRT

<213> Artificial Sequence

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<223> Made in a lab

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Phe Asp Lys Ser Asp Leu Ala Lys Tyr Ser Ala

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5

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